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CLINIC OF DR HENRY A CHRISTIAN

PETER BENT BRIGHAM HOSPITAL

SOME CLINICAL SIMILARITIES BETWEEN PATIENTS WITH PERNICIOUS ANEMIA AND THOSE WITH POLYCYTHEMIA

TODAY before showing you the patient I am going to give you in brief his history and discuss it from the point of view of diagnosis The patient, Med No 23,205, is a man fifty-five years old He was admitted to the Peter Bent Brigham Hospital on March 6, 1924, complaining of weakness, dyspnea on exertion, gas on the stomach, and an uncomfortable sensation in the epigastrium after meals His family history and past history are entirely negative as regards any relation to his present condition His present illness appears to date back three years, when the patient began to have distress after meals, a sensation of weight in the epigastrium, and a lump in the throat Since that time he has noticed an increasing weakness, and for the past eight months he has been tired for almost all of the time Sometimes for three to four days he will feel fairly well, and then his symptoms will recur and his gastric complaints become worse For the past eight weeks he has had shortness of breath on exertion and weakness Six weeks ago the dyspnea became so marked that he was obliged to resign his position as cantor in the Synagogue because he could not sing well any more At times he has noticed a prickling sensation in his toes Notwithstanding these symptoms he has not been confined to his bed

The symptoms complained of by this patient point to a possible cardiac weakness of some sort or to some defect in the blood responsible for the weakness and dyspnea With cardiac insufficiency one often gets symptoms referred to the stomach of one sort or another In most cases of cardiac insufficiency dypsnea is a more prominent symptom than weakness, and the dyspnea antedates the gastric disturbances rather than the gastric disturbances preceding for a considerable period of time the dyspnea and weakness as occurred in this patient

As already suggested, a defective blood-content, particularly anemia of some sort, would readily explain the weakness, and the anemia, if marked, would explain the dyspnea Also it is true that associated with anemia, and often among its early symptoms, are a variety of gastro-intestinal symptoms You will note that this patient complained, too, of a prickling sensation in his toes, such sensory disturbances, particularly in the hands but sometimes in the feet, very frequently occur in patients with anemia

Now if this patient has cardiac insufficiency, one would expect when he is seen that he would show cyanosis, evidence of a cardiac lesion, and some signs of edema On the contrary, if he has anemia, pallor rather than cynosis will be found, there will be little evidence of any cardiac lesion, edema may be present, though it is apt to be slight An examination of the blood will quickly determine the presence or absence of anemia

Now let us see what the appearance of the patient is and what we find on physical examination In the first place, he shows a striking cyanosis, which is particularly marked in the mucous membrane of his lips, tongue, and mouth Though marked, it is less evident in his fingers, hands, and ears, still less in his face and feet, and relatively little marked over the rest of his body The patient is lying flat in bed, with no evident respiratory discomfort, which fact is out of proportion to his appearance of cyanosis had he a cardiac insufficiency of sufficient degree to produce the cyanosis His heart is slightly enlarged, the sounds are normal without murmurs The pulse is absolutely irregular The walls of his larger arteries show

thickening, some tortuosity, and some evidence of irregularity The fingers show slight clubbing It is evident at a glance that he has no anemia He does present some evidence of cardiac disturbance in the absolutely irregular pulse, which electrocardiograms show to be auricular fibrillation and auricular flutter There is no subcutaneous edema, however, and no accumulation of fluid in his pleural or abdominal cavities His blood-pressure is within normal range Further examination shows that his liver edge is palpable well below the costal margin, and that his spleen is easily felt with a thick rounded edge two fingers below the costal margin

Taking up the results of a study of his blood, instead of an anemia we find that he has an excessive amount of hemoglobin, the estimates ranging from 150 to 170 per cent, a much increased red blood-cell count, varying between 8,730,000 and 10,770,000 and an increased white blood-cell count, varying between 10,450 and 18,900 The blood-picture is typically that of polycythemia It is a striking thing that in this case with so much in the history to suggest an anemia his blood shows the reverse condition—a polycythemia

Let us turn to a description of the symptoms found in patients with polycythemia and see how far their symptomatology, as described by those who have studied the disease, simulates those found in pernicious anemia Fitz, in Oxford Medicine, Vol II, p 763, discussing polycythemia, and using the term "erythremia" for this type, says[1] "Such general symptoms as weakness, lassitude, loss of weight, shortness of breath on exertion ease of fatigue, and somnolence are common Pain in the legs may be a striking symptom, occurring as violent muscular spasm or in the form of paresthesia with hyperhidrosis The pain may be so severe as to keep the patient awake at night and may be accompanied by swelling around the large joints suggesting infectious arthritis The digestive system is often involved Obstinate constipation is common, as is loss of appetite, feeling of fulness in the stomach, and attacks

[1] In these quotations the author's order of sequence of sentences is not followed at all times and parts are omitted

of vomiting without relation to meals Eye symptoms are common and frequently the first noted, the patient complaining of blurring of vision or that he is disturbed by specks before his eyes His mentality may be abnormal, with periods of irritability and depression, or the speech may be embarrassed and the memory poor"

Let us contrast this with a description of the symptoms of pernicious anemia Minot in the same work, page 514, says: "General weakness or abnormal fatigue are the commonest symptoms of which the patient is apt to complain There are certain symptoms that are more or less peculiar to pernicious anemia These are symptoms referable to the gastrointestinal tract, especially a periodic sore tongue and mouth, and to the central nervous system, especially a persistent paresthesia of the hands and feet and symptoms of combined sclerosis" Describing a little bit more in detail symptoms referable to the stomach and intestines, he says, "They are loss of appetite, nausea, vomiting, and diarrhea, paroxysms of which are more or less prominent At times there is diarrhea alternating with constipation, while in some instances constipation alone is prominent Indefinite abdominal pain with a sense of fulness, pressure, and distention, usually associated with the passage of an excessive amount of gas and often putrefactive stools, commonly occur There occur also frequent paroxysms of abdominal pain with or without diarrhea" In another place he says, "Symptoms, as muscular weakness, dyspnea, palpitation, vertigo and fainting, of course, occur Edema may also develop, particularly in the feet Symptoms referable to the circulatory apparatus are sometimes the first ones of which the patient complains" Cabot in Modern Medicine, Vol IV, p 629, says, "Dyspnea was present in 800 out of 915 cases of pernicious anemia, but palpitation occurred in almost every case," indicative of the great frequency of these circulatory symptoms At autopsy on cases of pernicious anemia there is usually found a definite cardiac hypertrophy

Reviewing 10 other patients with polycythemia studied at the Peter Bent Brigham Hospital, this same group of symp-

toms—weakness, palpitation, gastro-intestinal complaints, and sensory disturbances—quite dominate their histories In only 1 were these absent In 6 weakness was complained of as being present in some form, 2 mentioned palpitation, 1 dyspnea, 1 described burning eructations another nervous indigestion, another nausea still another vomiting 1 pain in the stomach region, and another a gnawing sensation, dizziness was complained of by 3 and 3 had headaches, 1 spoke of paresthesias in the fingers lasting a few minutes, another had numbness on one side of the body, another grinding pain all over the body, but especially from the hips to knees, still another had numbness from the hips to the knees, 1 said there was a sensation of burning and swelling in the hands, while another described a sensation as if at times walking on air Possibly if symptoms of this group had been associated in the minds of those taking the histories with polycythemia as closely as they are with pernicious anemia, these 10 histories of polycythemic patients would have shown a greater incidence of weakness, dizziness, gastro-intestinal symptoms, and sensory disturbances As it is, they are frequent and many of these histories are strikingly similar to those of patients with pernicious anemia

In pernicious anemia free hydrochloric acid is practically always absent from the gastric juice In 4 of our patients with polycythemia a gastric analysis was made by the fractional method at twenty-minute intervals following an Ewald test-meal The results in these 4 patients were as follows Case I first specimen, free hydrochloric acid 8, total acidity 34, second specimen, free hydrochloric acid 24, total acidity 66, third specimen, free hydrochloric acid 37, total acidity 64, Case II, first specimen, free hydrochloric acid 28, total acidity 56, second specimen, free hydrochloric acid 62, total acidity 90, third specimen, free hydrochloric acid 50, total acidity 70, Case III, first specimen, free hydrochloric acid 4, total acidity 6, second specimen, free hydrochloric acid 0, total acidity 18, third specimen, free hydrochloric acid 0, total acidity 18, Case IV, first specimen, free hydrochloric acid 40, total acidity 52, second specimen, free hydrochloric acid 41, total acidity 65, third

specimen, free hydrochloric acid 48, total acidity 57 In all free hydrochloric acid was present in the polycythemic patients, though it was small in amount in one of them Though both groups of patients very generally complain of gastric symptoms, these findings in the 4 patients with polycythemia indicate that the gastric juice in polycythemic patients is fairly normal or slightly hyperacid in sharp contrast to the hypo-acidity and achlorhydria of pernicious anemia

Two blood conditions so diametrically opposite as polycythemia and pernicious anemia, as here emphasized, cause very similar symptoms If both too little and too much blood can cause similar symptoms, perhaps the blood change is only a partial explanation of the abnormal conditions that are found and relatively, after all, unimportant Often it has been pointed out that the central nervous system symptoms, so regularly found with pernicious anemia, do not parallel the degree of anemia, they may be very marked with slight degrees of anemia and very slight in extremely anemic patients This has suggested that this group of symptoms is caused by the same toxic condition responsible for the anemia and does not result from the anemia itself The same may be true of other symptoms of pernicious anemia In a similar way symptoms of polycythemia might be explained At any rate it is difficult to understand just how they could result from the excess of red blood-cells

Some patients with polycythemia pass over into a stage of anemia and then present a blood-picture much like pernicious anemia so far as red cells are concerned These changes are described by Minot and Buckman (Amer Jour Med Sci, 1923, clxvi, 472) as follows "In all cases coincident with the development of the anemia, striking pathologic changes were observed in the peripheral blood During the period of anemia the red cells showed marked variation in size and considerable variation in shape Microcytes were evident, though never in profusion Macrocytes of abnormal shapes occurred, and true megalocytes In one blood these were very plentiful, so that the red-cell picture resembled that of a typical case of pernicious anemia, while the red-cell picture in all 3 cases sug-

gested this disease The unevenness in the depth of staining of the cells was usually striking The numbers of polychromatophilic cells varied, as did the reticulocytes Considerable increases were frequently observed Various types of nuclear remains are present Blasts were a feature, as many as 3000 per cubic centimeter were seen All types were present, including some showing divided nuclei With progression of the disease more of these immature elements appeared in the blood stream " Even when the count is above normal the cells may show some of the appearances found in pernicious anemia This suggests further that there may be some fundamental similarity other than a similarity in symptomatology between these two conditions, polycythemia and pernicious anemia

CLINIC OF DR GEORGE R MINOT

COLLIS P HUNTINGTON MEMORIAL HOSPITAL OF HARVARD UNIVERSITY

A CASE OF GENERALIZED ENLARGEMENT OF LYMPH-NODES AND HYPERTROPHY OF SPLEEN ASSOCIATED WITH CHRONIC FOCAL INFECTION

The Importance of Habit in the Regulation of the Bowels, Remarks Concerning the Fatal Diseases of the Lymphoid Tissue

INTRODUCTION

A PATIENT presenting a generalized and considerable enlargement of the lymph-nodes of the body and a spleen that is palpable, in the absence of an acute infectious disease, as a rule, will be found to suffer from a serious and fatal condition The correct diagnosis usually will be either Hodgkin's disease, lymphosarcoma, or some form of leukemia—malignant lymphomatous conditions Tuberculosis, syphilis, trypanosomiasis and other tropical disorders can give such a picture and, rarely, Gaucher's disease and extensive metastatic carcinoma and endothelioma Infectious mononucleosis, an acute condition from which recovery occurs, and which is not to be confused with leukemia, may present the manifestations mentioned Very seldom splenic anemia, known in its late stage as Banti's disease, perhaps presents slight swelling of the different groups of superficial lymph-nodes

Localized enlargement of lymph-nodes due to an infected focus, such as the tonsil is common Very little consideration appears to have been given to chronic pyogenic infection as the cause of a generalized and considerable enlargement of the lymphoid tissue

I wish to point out to you that there are cases with chronic focal infection that recover after having for a long period of time swollen lymph-nodes in different parts of the body, enlargement of the spleen, and alterations in the formed elements of the blood. I have had opportunity to observe at least 5 cases that appear to be of this type They were all adolescent males and had chronic infection of the tonsils or accessory nasal sinuses, frequently both This type of case should be distinguished particularly from those it resembles most, namely, cases of different types of incurable disease of the lymphoid tissue with alterations in the blood

THE PATIENT

The young man with excellent physique who stands before you is twenty-three years of age, 6 feet tall, and weighs 176 pounds During the past five years he has been in splendid health and without any detectable abnormality He is one of the 5 cases just referred to Seven years ago, when he was first seen, he presented a very different picture At that time he weighed 138 pounds, and was about 3 inches shorter in stature, appeared somewhat pale, and at once gave one the impression of being in poor health

History.—The history obtained seven years ago, when he was a school boy, as well as the record of his physical examination, is as follows

"A year ago he had scarlet fever without known complications Since then, but particularly in the past two months, he has been increasingly abnormally tired, and has lacked strength, but not to a degree to prevent him from playing baseball, tennis, and the like His scholastic ability has always been excellent and, in spite of an increase of irritability, he has continued to rank high in his class It is believed that he 'gets winded more easily than a year ago,' and on account of this and the lack of sense of well-being a physician's advice was sought

"In the past three months his appetite has not been good, but he has eaten enough to maintain, though not to gain, weight. In the eight months before his appetite began to fail he gained

10 pounds Prior to four months ago his bowels moved with perfect regularity About that time a relative believed the boy required catharsis and had him take some purgative preparation every few days It was then suggested to him by a physician that he should omit the cathartic, but he found that 'his bowels would not move unless he took a pill each night' Thus, he has taken daily in the past two months some laxative medicine During this time he has drunk a large amount of milk, which 'has caused him to dislike fruits and vegetables' and thus these foods have been eaten much more sparingly than heretofore He has taken appropriate amounts of the ordinary concentrated carbohydrate foods and suitable amounts of meat, poultry, and fish, but rather sparingly of foods with a high fat content Since cathartics have been considered necessary, intestinal gas, recurring mild abdominal discomfort, and slight nausea have become bothersome Likewise, the stools have been passed at different times of day instead of as formerly at the same hour each day

"At the ages of eleven and twelve he had mild attacks of tonsillitis and since then has been subject to 'head colds,' not less than four occurring every year In the past nine months he has had more or less constantly what he terms a 'cold in his head' His symptoms have been those one associates with a chronic nasopharyngeal catarrh and he has not been able to breathe freely through his nose especially at night There have been several periods of many successive days when he blew from his nose thick yellowish material, more particularly toward the end of the morning This has seemed to come rather more from the left than the right nostril There has been no pain

"Upon discovering large lymph-nodes in the groins the patient stated that he believed they had been of their present size for at least three years Shortly after recovery from scarlet fever nodes in both sides of his neck were noted and he considers that they have increased in size and number within recent months These enlarged lymph-nodes have bothered him in no manner nor given him cause for worry

"Questions were asked referable to all the systems of the body, and no further positive information was elicited than that given above

"He had measles at the age of seven, but no other illness or ailment of any sort can be recalled until scarlet fever occurred a year ago There is no information to suggest contact with tuberculosis

"The *family history* shows that he comes from a healthy stock His grandparents all lived beyond the age of seventy. His father and mother, the latter being an only child, are well One paternal uncle died at the age of fifty of cancer. Two others, over sixty years of age, are in robust health His only brother, aged twenty-two, is a college athlete"

Physical Examination.—The physical examination made seven years ago showed "A well-developed, intelligent, quickly responsive boy whose weight and height have been given. Pallor and sallowness, both slight, are evident. The facies, though broad, show a slightly drawn expression, and there is a tendency to breathe through the mouth A nose and throat specialist considers the tonsils and adenoids of 'moderate size' and not definitely infected There is apparently no increase of lymphoid tissue in the pharynx No tenderness over the accessory nasal sinuses is detected The roentgenologist interprets *radiographs* to show a slight opacity of the left anterior ethmoid cells which extends to the maxillary antrum Here there is distinctly more opacity when compared to the right. However, there is not sufficient evidence from the Roentgen-ray examination, taken together with the clinical examination, including transillumination, to warrant a diagnosis of sinus infection, at least of a degree to make surgical intervention desirable It is believed that a subacute rhinitis is present and that the nasal discharge has been rather slight

"The *lymph-nodes* that are palpable are discrete, firm, non-adherent, and not tender In the posterior and lateral aspects of the neck there occur chains of many bean-sized nodes and a few as large as 3 5 by 1 5 cm Anteriorly, on the right, pea-sized nodes are palpable readily and on the left there are a few

four times this size Just above the outer part of the left clavicle, situated deeply, are two nodes measuring about 4 5 by 2 cm Two large pea-sized nodes can be felt directly over the left mastoid process of the skull In both axillæ a small bunch of nodes is felt On the left side the mass is composed of at least nine different nodes, the largest the size of a large English walnut, the smallest no larger than the eraser of an ordinary lead pencil The few on the right are on the average 2 5 by 1 cm In the groins there are many nodes varying in size from that of a large green olive to those one-fifth as large

"The *abdomen* is slightly distended, but nowhere tender A considerable amount of fluid and soft solid material—evidently fecal—is present in the right lower quadrant There seems to be an ill-defined mass in this region which, perhaps, is composed of enlarged lymph-nodes The *spleen*, with its characteristic, firm edge and notch, is felt readily 4 cm below the costal margin, descending further upon forced respiratory inspiration No other organs or abnormal structures are felt within the abdomen

"The *thoracic organs*, *blood-pressure*, *eyes*, *reflexes*, *bones*, and *teeth* appear normal

"A *Roentgen-ray examination* of the thorax reveals the existence of a considerable amount (at least twice as much as seen in most healthy people) of peribronchical thickening in the form of masses of nodes situated near the base of the heart These nodes are not calcified and though definitely abnormal their contour is not notched or lobed as occurs often in Hodgkin's disease The lungs and heart appear normal

"The *urine* is normal

"The *stools* are mushy and not formed, acid in odor and reaction, but otherwise normal

"The *blood* was examined several times during the ten days after the boy was first seen The analysis always showed essentially the same picture, as follows

"*Hemoglobin*, 75 per cent"

Red blood-corpuscles, 4,100,000 per cubic millimeter These cells were slightly achromic and varied in size abnormally,

but not markedly Cells half the size of normal were not unusual and a microcyte was seen rarely, but macrocytes were absent Somewhat narrow oval-ended cells occurred, otherwise the cells conformed quite well to normal shape There were no nucleated red cells, but polychromatophilia was observed and the reticulocytes formed 1 5 per cent of the red blood-corpuscles

The *blood-platelets* were increased moderately Rarely an abnormally large and granular one was seen

The *white corpuscle* count varied from 10,000 to 14,000 per cubic millimeter

The differential count showed

	Per cent
Polymorphonuclear neutrophils	53 5
Polymorphonuclear basophils	1 5
Polymorphonuclear eosinophils	2 5
Lymphocytes—small	28 0
Lymphocytes—atypical	6 0
Large mononuclears	8 5
	100 0

The *blood clotted* in normal time and the clot retracted in normal fashion The serum contained a slight excess of bile pigments

The *Wassermann reaction* on the blood-serum, the *fasting blood-sugar*, and *non-protein nitrogen* of the blood were normal

Treatment Seven Years Ago The Importance of Habit in Regulation of the Bowels—Following the attempt to discover the nature of his affection it was thought that a form of serious disease of the lymphoid tissue was probable, but that this was not so and need not have been believed to be true will be pointed out later The welfare of the patient must have always foremost consideration, and in unusual cases peculiar features are apt to overshadow the simpler aspects This boy's lymph-nodes and blood, neither of which bothered him, interested the physicians so much that the state of the intestinal tract, which could be responsible for some of his lack of sense of well-being, was almost forgotten It is, of course, most desirable that you approach each case as a new scientific problem and make the

fullest use of an inquiring mind but the patient, not a separate feature of his case, must be the center of all interest

This boy illustrates the ease with which people may obtain the habit of taking purgative preparations, a bad habit often encouraged by the many advertisements of cathartics in daily papers The gross character of the patient's stool, its acid odor, and reaction were quite certainly due to catharsis It is, of course, no novelty today to see many people purging themselves regularly , just as they used to bleed themselves a hundred years ago The habit is apt to start following some minor ailment or when the bowels are thought to be functioning improperly Then a continued lack of a sense of well-being is attributed to costiveness, more laxatives are taken, leading only to an aggravation of the intestinal difficulty which often permits a continued sense of ill health The need of defecation is normally established by the accumulation of feces in the rectum This physiologic stimulus is regulated by habit and the lack of establishing a habit of going to the toilet at a fixed hour is often the sole cause of constipation, a fact well described by John Locke in the seventeenth century, yet now so often not appreciated After breakfast is the ideal time for the bowels to move, as then the intestine has received not only the stimulus of food through the gastrocolic reflex, but also the influence of physical motion following rest The will has a definite effect on defecation, while the voluntary bringing into play of abdominal pressure aids the function and induces peristalsis Plenty of food, particularly generous amounts of vegetables and fruit serve to regulate intestinal function In many people, all that is necessary to cure their constipation is to persuade them to recognize the importance of habit and training This boy's attention was drawn to the inconveniences of laxatives and they were prohibited In was pointed out in a convincing manner that one always succeeds by intelligent treatment, which is training and habit He was ordered to take a large breakfast slowly and then go to the toilet, allowing plenty of time for the bowels to move whether he had the desire or not It was explained to him that he must go at no other time and refuse to let his

bowels move except at the appointed hour The careful selection of nature's laxative foods and exclusion of those enhancing constipation is often of much importance in restoring the occurrence of a daily normal stool Various non-drug-like substances to increase bulk and to soften the excreta may be most helpful Habit, however, is of prime importance In spite of poor appetite, the boy felt he could take a copious diet, which was explained as advantageous He was asked to decrease the amount of milk, as this food tends to be constipating. In turn, he was requested to give preference to fruit and vegetables, but so as not to overdirect his attention to what he ate, no great excesses of these foods were ordered These simple directions will succeed in many cases, but unfortunately too often the effects of countersuggestions cause failure Success does not result unless the physician takes ample time and pains to indicate that the idea of failure is not to be considered, and carefully explains the reasons for these simple measures and persuades the patient to follow them out seriously A sedentary life, of course, favors constipation, even a little exercise each day, as a brisk half-hour walk, is of great advantage in alleviating this common complaint A few days after this boy stopped his cathartic medicine and had followed the principles outlined above his bowels moved regularly, and he has continued ever since in these past seven years to have daily a normal formed stool His ill-defined abdominal discomforts soon ceased, his appetite improved at once and in two weeks he felt much better in general At this time the only other advice given was that he obtain rather more rest and less exercise than formerly, and a simple cleansing solution was prescribed for his nasopharynx

The Course of the Case in the Next Two Years.—When the patient returned two months later he looked distinctly better, was neither pale nor sallow, felt well, and had gained 4 pounds The discharge from the nose stopped within two weeks after leaving the hospital There was no change in the size of the lymph-nodes or spleen The hemoglobin had risen to 90 per cent and the red cells appeared normal The plate-

lets remained slightly increased The white count was 8000 per cubic millimeter and the differential count showed more bone-marrow elements and fewer lymphocytes than when he was first seen yet the latter remained rather high

During the next six months this patient remained apparently well and yet there was no change in the size of the lymph-nodes or spleen He was then not seen until eight months later *i. e.*, sixteen months after the original study At that time it was learned that in the preceding six months he had not felt strong and had got tired easily His relatives had noted that he slept with his mouth open and that for at least four months had appeared to have a "a cold most of the time and blew his nose frequently" He spoke of a sense of fulness above the nose, but of no pain in any part of the head His family was quite aware that his voice had become of a type associated with nasal obstruction and it was evident to the physicians that his speech had more of a nasal twang than formerly Upon examination the tonsils and adenoid tissue of the nasopharynx were found definitely infected and hypertrophied Tissue in the region of the left middle turbinate bone caused obstruction No definite evidence of sinus infection was obtained though Roentgen-ray examination did show that the opacity previously noted was still present The spleen remained of the same size The lymph-nodes in the different chains of the neck were undoubtedly somewhat larger and more numerous but the large node in the left axilla had decreased to half its former size The amount of peribronchial thickening as told by Roentgen-ray examination seemed to have increased The patient had neither lost nor gained weight though he had grown an inch taller

The boy appeared at least as pale as when he was first seen and the *hemoglobin* was 75 per cent The *red cells* had again become somewhat achromic and microcytes appeared in the blood though they were few The *platelets* were increased, their numbers being 600,000 per cubic millimeter Several observations showed the *white corpuscles* to be in the vicinity of 12,000 per cubic millimeter The average differential count at this time was as follows

	Per cent
Polymorphonuclear neutrophils	45 0
Polymorphonuclear basophils	2 5
Polymorphonuclear eosinophils	2 0
Lymphocytes—small	32 5
Lymphocytes—atypical	8 0
Large mononuclears	10 0
	100 0

There was no fever and the pulse-rate averaged 78 beats per minute

A lymph-node was removed from the neck The pathologic examination was considered to show only chronic inflammatory hyperplasia The lymphoid tissue was richly cellular, the cells varied somewhat from normal type but not sufficiently to warrant a diagnosis of some form of malignant lymphoma The sinuses contained many endothelial cells Hyperplasia of lymphoid cells occurs early in the nodes of persons afflicted with Hodgkin's disease, but as the process develops, among other features, the nodes lose their architectural identity The lymph-node from this boy did show some obscurity of the natural structure of a lymph-node but, by and large, the different parts retained their individuality I do not intend to discuss the pathology, but wish you to realize that the response to irritation and the relatively mobile character of lymphoid tissue renders difficult the interpretation of its hyperplasia Thus divergent views and confusion exist concerning the numerous conditions characterized by distinct abnormalities of the lymph-nodes

The patient's tonsils and lymphoid tissue in the naso pharynx were excised These tissues showed marked chronic inflammatory changes, but there was no evidence of lymphoma The surgeon also removed a portion of the left middle turbinate At operation a slight amount of watery material was observed to come from the region of the ethmoid cells and both maxillary antra Ten days later the boy left the hospital At this time the polynuclear neutrophils had increased a little and the lymphocytes had decreased

He was not seen again until six months after the operation,

when he felt and looked exceedingly well and had gained 10 pounds in weight. In spite of the slight signs pointing to infection of the accessory sinuses, it is believed they had been definitely infected This assumption is borne out by the fact that the Roentgen-ray examination of the sinuses six months after operation showed the opacity, noted before to be practically gone At this time the spleen could not be felt, even after the patient had taken a very deep breath while lying on his right side All the lymph-nodes were much smaller than before, none being larger than peas or small beans The *blood* showed no abnormality of the red cells or platelets The *white count* was 7000 and the differential count as follows

	Per cent.
Polymorphonuclear neutrophils	64 0
Polymorphonuclear basophils	0 3
Polymorphonuclear eosinophils	1 0
Lymphocytes—small	28 0
Lymphocytes—atypical	1 0
Large mononuclears	5 6
	100 0

The Patient at Present.—It is now almost six years since the operation and he has continued to enjoy good health and has appeared very well, as you see that he does today Now one cannot palpate lymph-nodes in the axillæ and except for a few tiny ones in the left neck no others are felt in this region Those in the groins are palpable, but smaller than formerly and no larger than nodes to be felt in many healthy men The spleen is not felt The blood-picture is entirely normal

DIFFERENTIAL DIAGNOSIS

The lymphoid tissue of the body is much more prominent in youth than in the maturer years of life and seems more vulnerable in the young than in the old It also appears to be more susceptible to disease in males than in females and, as is well known, Hodgkin's disease is particularly an ailment of young males This patient's age and sex were such that this malady was suspected when he was first seen Hodgkin's disease usu-

ally becomes apparent with enlargement of a group of nodes, particularly in the cervical region, and extension usually takes place slowly However, rapid extension may occur and general lymph-node and splenic enlargement may appear soon Following the stimulative reaction shown by the lymphoid tissue at the very beginning of Hodgkin's disease there is evidence of a destructive action on the lymphocytes by a strong lymphotoxin Thus after this fatal disease is established, a gradually decreasing percentage of the lymphocytes in the blood occurs throughout life as has been so well pointed out by Bunting The eosinophils become increased, but later decrease Basophils are present, but tend to vanish as lymphopenia becomes marked An increase of large mononuclear cells is the rule throughout the disease Very early the stimulative reaction is reflected in the blood by an increase of lymphocytes, but this increase is transient and does not occur when the morbid state is present in many groups of nodes Hence, such a general enlargement of the lymph-nodes as this boy showed, taken together with his blood-picture, is not in accord with the diagnosis of Hodgkin's disease Likewise, when a generalized enlargement of lymph nodes occurs in Hodgkin's disease, they will be found, on the average, larger and the patient sicker

The rare chronic generalized hyperplastic form of tuberculous lymphadenitis may closely resemble Hodgkin's disease The more usual form of lymph-node tuberculosis with caseation, softening, and matting together of nodes should cause no confusion The blood-picture in tuberculosis of the lymph-nodes, unless of a malignant rapidly caseating type shows a relatively high lymphocyte count, a low eosinophil, basophil, and large mononuclear count Thus the blood-picture in the chronic hyperplastic form of tuberculosis is entirely similar to that seen in early, but not in established, Hodgkin's disease The patient's blood showed more eosinophils, basophils, and large mononuclears than are to be expected with tuberculosis Clinically, he did not resemble a patient with tuberculosis, he had no fever, no rapid pulse, and no history to suggest this disease, though the early gastro-intestinal symptoms and lack of sense

of well-being might have been considered due to tuberculous toxemia The Roentgen-ray findings in the chest were not considered to resemble tuberculosis, there not even being calcified nodes so commonly seen when this disease is present The progress of his case did not resemble that of tuberculosis, nor did the pathologic examination of the node in any way suggest it

The patient's blood-picture rules out, of course ordinary leukemia Pseudoleukemia, *i c*, aleukemic lymphocytic or lymphoblastic leukemia, forms of lymphoblastoma, present concurrent enlargement of different groups of nodes more often than Hodgkin's disease It occurs typically in elderly males and is looked upon by some as the response of the adult to the same cause that produces typical Hodgkin's in youth The condition is progressive the groups of lymph-nodes often massive, and yet it is not unusual to find the external nodes but trivially or not at all enlarged The white cells may be slightly increased but leukopenia is not unusual The lymphocytes usually are found continually in a high, but not in a greatly increased percentage Atypical lymphocytes are present, as a rule, and sometimes occur in large numbers The eosinophils are apt to be higher than in tuberculosis, there being 2 to 3 per cent, basophils are usually found and large mononuclears may be slightly increased

This type of leukemia could not be definitely ruled out when the patient was first seen, but as this condition is progressive and seldom lasts five years the course of the case as well as the pathology found, clearly indicates no such disease existed

Early Banti's disease—splenic anemia—may give a blood picture resembling that of early Hodgkin's disease Leukopenia soon becomes a feature and the blood may suggest a form of aleukemia Banti's disease very rarely shows swelling of the superficial lymph-nodes and probably only when the condition is advanced and leukopenia evident Thus this condition was ruled out when the patient first came under observation

Lymphosarcoma, clearly differentiated from Hodgkin's and aleukemia by some and not sharply distinguished by others was excluded by the general nature of the case and definitely so by the pathologic examination of the node and tonsils Lym-

phosarcoma may be impossible to differentiate from Hodgkin's disease, except by microscopic examination of tissue The blood-picture seems variable, it sometimes resembles that of early Hodgkin's disease and also aleukemic leukemia A high percentage of large mononuclears is common Clinically, involvement of the tonsils, the gastro-intestinal tract, serous surfaces of pleura and peritoneum, and the invasion of surrounding tissue are characteristic of lymphosarcoma rather than of Hodgkin's disease When the disease is especially localized in the mediastinum or abdomen, the patients often present obscure symptoms and fever, and may soon become very sick

There is, of course, nothing to suggest that this boy had syphilis, some form of metastatic malignant tumor, or a tropical disorder as trypanosomiasis, which conditions may cause generalized hypertrophy of lymph-nodes Infectious mononucleosis, or glandular fever, is an acute condition typically occurring in youth, with a generalized adenitis and splenic enlargement Lymphocytosis, with the occurrence of many atypical lymphocytes and mononuclear cells, is a feature The white cell picture is often abnormal for less than three weeks, but may remain somewhat pathologic for even three months Although this boy's blood-picture may perhaps have resembled that seen during convalescence from this condition, there was no acute phase of his illness, nor did he have fever, so there was no reason to consider that he had infectious mononucleosis Likewise the alterations in his blood persisted much longer than is reported to occur in such cases

FURTHER CONSIDERATION OF DIAGNOSIS AND DISEASE OF LYMPHOID TISSUE

Localized adenopathy due to acute or chronic infection is of common occurrence A generalized relatively slight lymphadenitis occurs in a variety of infections, such as chicken-pox, measles, scarlet fever, typhoid fever, etc, diseases that especially occur in youth, a time when lymphatic tissue seems particularly vulnerable, also in non-infectious conditions an increase in the bulk of the lymphoid tissue throughout the body

may occur as in exophthalmic goiter The reaction of the lymphoid tissue may be shown in the blood, for example, in chicken-pox the white cell picture may be like that seen in infectious mononucleosis, and lymphocytosis may occur in exophthalmic goiter This boy had scarlet fever a year before he was first seen and it is possible that some enlargement of his lymph-nodes may have been due to this disease, or that as a result of it they became especially susceptible to injury However, the size of the nodes and the spleen and the subsequent outcome indicate that scarlet fever alone was not probably the important cause of his adenopathy It is evident that he had been subjected to a lymphotoxic agency and the course of his case, comparable to that of others, certainly strongly suggests that the source of the abnormalities was from chronic infection in the upper respiratory tract The lymphocytosis and occurrence of abnormal lymphocytes reflect the influence of a lymphotoxin and his blood-picture was similar to that which may be seen in pseudoleukemia Bunting has pointed out that with chronic nasal sinus infection it is the rule to find all forms of white cells increased, except the polynuclear neutrophils I too, have often seen this picture in such cases and believe it may persist for a very long time The increase of basophils may be a striking feature This boy's leukocyte formula approached this character and, although there was considered to be rather little evidence of sinus infection on physical examination, the Roentgen-ray examinations and nature of the patient's symptoms seem to indicate that there was chronic sinus disease in addition to chronic infection of tonsils and adenoids

Lymphocytosis, relative and absolute, with other but varying changes in the blood-picture, occurs, of course, in other pathologic states than those mentioned, as, for example, in infectious (catarrhal) jaundice and aplastic anemia, but there is no reason for these various other conditions to concern us, as they bear no real resemblance to this case

The patient's white cell picture was more abnormal when his symptoms were manifest than when absent, likewise, slight anemia and changes in the red cells appeared when nasal symp-

toms became evident The anemia can be accounted for readily as due to infection The slight degree of microcytosis that occurred suggests increased blood destruction, which is the rule in anemia due to chronic infection Anemia of some degree always develops in the different fatal diseases of the lymphoid tissue, but in the non-fatal condition infectious mononucleosis, anemia very rarely is observed This patient's anemia was a symptom that further permitted a similarity in his case to one of aleukemia and allied lymphoma The rather constant slight increase of his blood-platelets until he recovered indicates that there was an increased activity of their parent cells in the marrow, a desirable feature, indicating a good response of this tissue Increase of platelets and the presence of abnormal forms in the blood-stream is one of the features of the blood in Hodgkin's disease, which condition this patient most certainly did not have

Chronic infection of the upper respiratory tract is, of course, very common and a localized adenitis often accompanies it This patient illustrates, I believe, that occasionally such a condition causes a considerable generalized hyperplasia of the lymphoid tissue, more particularly at an age when this tissue is susceptible to damage Why it should occur in some and not in others offers opportunity for many speculations The same is true of the relation of Hodgkin's disease to focal infection A history of focal infection in the vicinity of the lymph nodes that first enlarge in Hodgkin's disease is common It is important not to neglect proper treatment of any infectious condition about the teeth, of the tonsils, sinuses, gastro-intestinal tract, etc , no matter whether irradiation or other special treatment is to be undertaken or not One may conceive theoretically of the same or related substance derived from infectious agents in different amounts, or in the same amounts, in differently susceptible people as producing variable pictures, in some but a simple localized lymphoid hyperplasia results, in others Hodgkin's disease, in still others generalized chronic lymphoid hyperplasia with the blood-picture this boy had and whose condition may be comparable to a chronic form of infectious mono-

nucleosis The nature of lymphomas and many lymphoid hyperplasias is unknown, the leukemic process appears like that of a malignant tumor, nevertheless, as Ewing notes, in different forms of lymphoma and lymphosarcoma "various processes appear active, some chiefly inflammatory, some neoplastic, and others intermediate in position" The apparently close relationships between the many forms of lymphoid hyperplasia, the occasional transformation of one to another, the complex anatomic structure of lymphoid tissue and lack of knowledge of etiology, which may be both infectious and neoplastic, makes interpretation of these fundamental diseases of the lymphoid tissue difficult An understanding of cases like this boy's offers one of many ways to increase knowledge about such morbid states Any other diagnosis than chronic focal infection to account for this patient's previous abnormal lymph-nodes, spleen and blood-picture is illogical

PROGNOSIS

Has enough time passed by to be sure that progressive fatal disease of the lymphoid tissue will not yet become apparent in this patient? Other than a positive answer to this question is unreasonable, because among other reasons not only has he appeared perfectly well for five and one-half years but also it is now over seven years since his first symptoms, and the serious diseases of the lymphoid tissue seldom last longer than this Even so, there are rare cases that do give a history of localized and even generalized swelling of lymph-nodes for many weeks, that then subside years before any signs occur of ill health due to a progressive lymphoma type of disease It is possible that in these individuals the lymphoid tissue is abnormally prone to disease, and hence one can conceive how this patient might develop more readily than another serious disease of the lymphoid tissue, but this seems most improbable

REMARKS CONCERNING THE ABDOMINAL AND BONE-MARROW LESIONS OF LYMPHOMA

It has been pointed out that an occasional case, which becomes entirely well, may resemble those with some serious form of lymphoma The resemblance is particularly because of enlargement of the spleen and lymph-nodes and alterations in the blood This may lead you to suppose that all cases of serious disease of the lymphoid tissue present readily detectable swelling of groups of external nodes As a matter of fact, most cases do so, but it is not rare to see them, even in an advanced stage of their disease, without evident enlargement of the lymph-nodes The patients may have both slowly and rapidly great spontaneous changes in the size of swollen lymphoid tissue A decrease usually, but not necessarily, heralds improvement in the patient's health Increase of internal lymphoid tissue, especially within the abdomen—often difficult to detect—can cause a great variety of mild and severe symptoms leading to the diagnosis of all sorts of abdominal, nerve, and bone conditions Such patients often suffer for a long time because the correct diagnosis is not suspected until external nodes or the spleen become hypertrophied or anemia develops In addition, the fever which is common in these lymphomatous diseases aids to mislead one The alleviation of abdominal pain, "sciatica," mild and severe backache, anemia, etc , due to pressure upon or invasion of abnormal structures by tumor-like tissue, is often striking and rapid following adequate Roentgen-ray or radium irradiation

Furthermore, the symptoms of marked anemia—pallor, weakness, dyspnea, palpitation, etc —may be the presenting ones in non-irradiated and irradiated cases of "lymphoma" without one being able to discover, at the time, any definite enlargement of the lymph-nodes or spleen The anemia, with or without irradiation treatment, may be progressive or lessen markedly, but only to return sooner or later

As noted before, anemia, sometimes extreme, becomes a feature in most typical and atypical cases of serious disease of the lymphoid tissue The decrease in hemoglobin and red

cells may be due not only to the deleterious effect on the marrow of some unknown toxic substance but also produced by the lymphomatous process invading the marrow In rare cases the tumor-like process in the marrow may predominate the picture and there be no evident swelling of lymphoid tissues It is such cases with symptoms of anemia that are confusing The blood-picture of these patients may be a striking one and may show many immature bone-marrow cells of all types In a recent case, with hemoglobin 50 per cent, and red blood-corpuscles 2,800,000 per cubic millimeter, the nucleated red cells formed 15 per cent of all nucleated cells in the blood-stream—12,000 per cubic millimeters The reticulocytes were 18 per cent, rather than about 1 per cent, as occurs in health A few myelocytes and atypical immature myeloid white cells were present This blood-picture can be accounted for readily, by the effect of abnormal growth within the marrow, forcing the normal immature elements into the circulation, just as may occur with bone-marrow metastases from any other type of malignant tumor Similarly in lymphatic leukemia, as the marrow becomes invaded, a few immature bone-marrow cells often appear in the blood-stream At the time this patient just referred to was observed first, there were no definitely enlarged external lymph-nodes however the spleen was slightly enlarged and some thought a mass of nodes could be felt in the right side of the abdomen A few weeks later the spleen became larger and two nodes the size of almonds appeared in the neck, but no others became swollen One of these was removed and examination under the microscope showed "malignant lymphoma"

In spite of the fact that it is common to observe bone-marrow lesions in malignant lymphomas, in most cases extensive rapid invasion of the marrow does not occur and the anemia is not associated with the striking blood-picture of a metastatic tumor of the marrow referred to above Even so, anemia and fever may be the main features of the case and enlargement of spleen and nodes slight or even apparently absent

In this hour I have touched upon numerous aspects of dis-

case of the lymphoid tissue and have hinted at the multiplicity of features for consideration and the complexity of the subject. In 1832 Hodgkin first clearly described the condition that bears his name and which was vaguely outlined by Malpighi in 1665 Bennett described leukemia in 1845, and between 1850 and 1865 Virchow, Wilkes, Wunderlich, and Cohnheim contributed important information about the diseases of the lymphoid tissue Since then much more knowledge has been advanced concerning these disorders Nevertheless, we do not know the cause of these conditions, their relation to each other, or a cure for them One of the big problems of modern medicine is to unravel the nature of these rather common fatal diseases that damage the lymphoid tissue

CLINIC OF DR FRANCIS W PEABODY

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CERTAIN CLINICAL ASPECTS OF PULMONARY EMPHYSEMA

THE patient for your consideration today illustrates a common and perplexing problem in diagnosis Dyspnea, and particularly dyspnea as the result of physical exertion, is the presenting symptom in a great many cases and may, of course, be due to a variety of pathologic conditions In a large proportion of patients it is readily apparent from the physical examination and from the clinical history that the shortness of breath is the result of cardiac disease In another large group it is quite evident that dyspnea is due to extensive inflammatory or infiltrative lesions of the lungs, such as tuberculosis or cancer, and in a smaller number of patients more unusual conditions, such as aneurysm and mediastinal tumor or a condition outside of the thorax are the obvious causes of the symptom There remains however, a considerable group of patients, most of whom are above middle age, in whom dyspnea is so marked as to interfere seriously with normal activity, but who show little or no evidence of heart disease and whose lungs are negative to physical examination except for the signs of emphysema In these instances the problem frequently resolves itself into a consideration of whether the dyspnea is due essentially to myocardial disease which has not developed so far as to produce the usual physical signs of chronic myocarditis—thus, whether the case is one of early myocardial failure, or whether the dyspnea is due primarily to an interference in the functional activity of the lungs depending on the pulmonary emphysema In many cases it seems most probable that each element plays a

rôle and that the dyspnea is due in part to myocardial weakness and in part to the emphysema Under such circumstances it is of clinical importance to determine the relative degree to which each of the factors contributes to the production of the dyspnea, but an accurate distinction is often difficult or impossible In many other cases it is quite evident that the cardiac element is predominant and is largely responsible for the shortness of breath In a smaller number of instances a careful study indicates that the cardiac features of the case are relatively insignificant and that the dyspnea depends on pulmonary emphysema It is the latter cases which most frequently pass unrecognized and they seem to be overlooked because of a lack of appreciation of the degree to which emphysema may interfere with the movements of the lungs and be responsible for shortness of breath

The patient before you is a business man about fifty years of age whose history was unimportant until 1918, when he had a serious attack of influenza during the epidemic Since that time he has had frequent colds during the winter and there has been an increasing tendency to the development of attacks of bronchitis which are sometimes slow in clearing up These attacks have never been serious, however, and, except for keeping him in bed for a few days, never interfere with his normal activities

Somewhat over a year ago he began to notice that he became short of breath more easily than formerly This became particularly noticeable last winter when he found that walking up any hill or even hurrying on level ground began to bother him He also noticed that his dyspnea was much more striking when he was walking with the wind in his face or in very cold weather During the last three months the tendency to dyspnea has increased, so he has had to walk much more slowly than formerly, and after ascending a short flight of stairs he has to pause to "catch" his breath Dyspnea is always associated with physical exertion He coughs when he first gets up in the morning and raises a little phlegm, but during the rest of the twenty-four hours cough is practically absent He has never noticed

pain in his chest and has had very little palpitation of the heart He sleeps poorly, but has not been bothered by shortness of breath while he is in bed His feet have never been swollen Otherwise except for a gradual loss of about 15 pounds during the last three years, his history is unimportant He states that if it were not for the increasing tendency to dyspnea on exertion, he would consider himself perfectly normal

On physical examination he is a tall, rather spare, healthy looking man Lips and conjunctivæ are of normal color and there is no cyanosis Physical examination is unimportant, except as it concerns the circulatory and respiratory system The cardiac impulse is not visible and on account of the resonance of the overlying lung, it is impossible to outline the area of cardiac dulness while the patient is lying down When he sits erect the left border of dulness in the fifth space is found to be 8 cm to the left of the sternum and about 2 cm inside the nipple line The heart is thus not enlarged to percussion Even in the erect posture the area of cardiac flatness remains entirely obliterated by pulmonary resonance There is no precordial hyperesthesia The action of the heart is regular at a rate of 85 Heart sounds are extremely indistinct at the apex and at the base The sounds are normal in character however, and no murmurs are heard Radial pulses are equal, regular, and of good quality Radial arteries are easily palpable, but apparently not calcified The temporal arteries are somewhat tortuous The systolic blood-pressure is 125 mm and the diastolic is 80 mm The chest is not barrel shaped but, on the contrary is flattened in the anteroposterior diameter Percussion note over both sides of the front of the chest is hyperresonant On the right this hyperresonant note extends practically to the axillary margin in the nipple line and to the ninth rib in the anterior axillary line The breath sounds are everywhere indistinct and expiration is slightly prolonged There are a few dry râles associated with inspiration Tactile fremitus is scarcely palpable In the back the percussion note is also hyperresonant The line of flatness indicating the lower border of the right lung is 14 cm below the angle of the scapula and the

lower border of the left lung is 15 cm below the angle of the scapula On the deepest inspiration there is scarcely any descent of the lung borders On auscultation the respiratory sounds and vocal fremitus are as in front The abdomen is normal throughout Examinations of the blood and urine are negative The vital capacity of the lungs is 2600 c c, which is approximately 60 per cent of the normal for a man of his height and weight After hopping sixty times on one foot the pulse-rate only increased from 84 to 100 and it returned promptly to its former rate, but the dyspnea was abnormally marked The electrocardiogram is entirely normal in form and does not suggest hypertrophy of either ventricle or a myocardial lesion x-Ray examination of the chest is negative It confirms percussion by demonstrating that the heart and aorta are not enlarged, and it shows that the lung fields are normal

One of the most striking features of this case is that the degree of dyspnea of which the patient complains is quite disproportionate to the physical findings in the examination of the heart It is, of course, common to see early cases of myocardial weakness in which the heart is essentially normal to physical examination, as well as to x-ray and electrocardiographic examination, but in which the limitation of the functional capacity of the heart shows itself by slight or moderate degrees of dyspnea on exertion In this patient, however, the degree of dyspnea is much greater, according to the history, and the evidence of the history is confirmed by the determination of the vital capacity of the lungs In general, one would expect that a man with a vital capacity of the lungs of 60 per cent of the normal would be able to walk slowly on the level, but would not be able to lead anything like a life of normal activity This is apparently just about the situation with our patient Were such a degree of dyspnea dependent on myocardial weakness one might well expect to find it associated with evidence of cardiac pathology, such as hypertrophy—indicated either by percussion, x-ray, or the electrocardiogram—murmurs, gallop rhythm, or abnormal complexes in the electrocardiogram, but none of these are present All of our methods of examining

the heart show normal findings Moreover, it is noteworthy that other symptoms of heart failure such as edema, cough, precordial pain, and palpitation, are either absent or insignificant. It is clearly difficult to explain the presenting symptom of marked dyspnea on exertion on the basis of the findings in the heart The general examination, however, reveals no condition outside of the chest which would explain the dyspnea

Let us now, therefore, consider the findings resulting from the examination of the lungs These findings indicate very little except a marked pulmonary emphysema The essential feature of the lungs in pulmonary emphysema is that they are voluminous, so that in the resting position at the end of normal quiet expiration—or at the so-called "Mittellage" the midpoint between normal expiration and inspiration—they approximate the condition of normal lungs toward the end of full inspiration The simplest method of demonstrating this increase in the size of the lungs is by percussion, which enables us to determine, somewhat roughly, their general outline What do we find? In the first place we find that the area of cardiac flatness is obliterated by the pulmonary resonance of overlying lung This, in itself, is not particularly significant, for it is found in many cases with little or even no emphysema Second, and more important, we find that the lower border of the right lung is almost at the costal margin It is thus at the position of the normal lung on full inspiration The lower border of the right lung can be determined with accuracy by percussing the line of flatness between lung and liver, but the lower border of the left lung cannot be accurately determined in front on account of the tympany of the underlying colon and stomach In the back the lower borders of both lungs can be determined by percussion, and instead of finding them about 8 or 9 cm below the angles of the scapulæ as is normal, they are found, in this patient, to be 14 and 15 cm below the angles of the scapulæ The lower borders posteriorly, with the lungs at rest, are thus in the position of the lower borders of normal lungs in full inspiration Moreover on percussing the lungs of our patient during full inspiration it is apparent that there

is no further descent of the lungs on deep breathing His lungs, at rest, fill the angles between the chest wall and the diaphragm, which are normally only filled by the lungs on deep inspiration. A further suggestion of emphysema is found in the hyperresonance of the percussion note The indistinctness of the breath sounds and the prolongation of expiration are characteristic of emphysema, but these signs are of much less value than the results of percussion. It is by means of percussion that we have shown that the lungs are voluminous and that they are definitely

DIAGRAM of LUNG VOLUMES

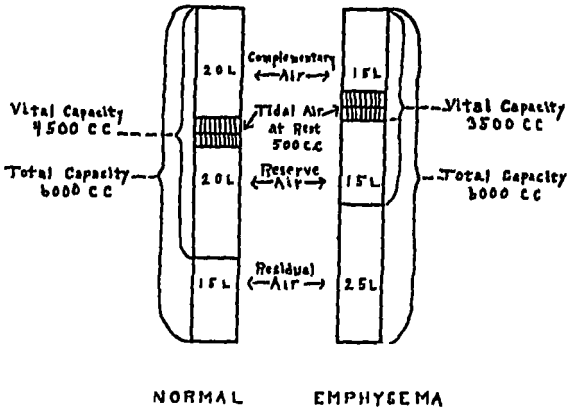

Fig 229

limited in respiratory excursion The barrel-shaped thorax, so commonly associated with emphysema, usually appears in long-standing cases, but here, as in many instances, is conspicuous by its absence

Further evidence, of a more quantitative nature, of the limitation of the movements of the lungs on inspiration and expiration is found in the determination of the vital capacity of the lungs, which is only 60 per cent of the normal Other, more complicated, measurements of the lung volumes would unquestionably confirm the results of percussion Figure 229

(adapted from Lundsgaard[1]), shows in diagrammatic form the relations of the lung volumes in emphysema to those under normal conditions It will be seen that the total lung volume (the volume of air in the lungs at the end of full inspiration) is approximately normal, but that the residual air (volume of air in the lungs at the end of complete expiration) is considerably above normal The vital capacity is decreased because of the increase of residual air, and at the middle position (midway between normal inspiration and expiration) the lungs contain an abnormally large quantity of air In very marked cases of emphysema Scott[2] has shown that interesting alterations in the chemistry of the blood take place as the result of emphysema The impairment of the respiratory epithelium may be assumed to cause an impediment to the exchange of gases in the lungs, for there is found to be an increase in the free carbon dioxid of blood, and, probably as a secondary process, an elevation of the combined carbon dioxid The relation between the two, however, remains unaltered, so that the H-ion concentration of the blood is within normal limits Scott says "The high level of free carbon dioxid of the blood in emphysema is attained gradually, so that ample time is afforded for the development of compensatory mechanisms The maintenance of the body bicarbonate at a permanent high level appears as one important illustration This enables the emphysematous subject to tolerate a high carbon-dioxid tension in the blood normally and also affords a certain protection against undue fluctuations in H-ion concentration which might otherwise occur from metabolism Considering the body bicarbonate as a chemical factor of safety, it appears that the emphysema subject can tolerate for short periods higher concentrations of inspired carbon dioxid than the normal When, however, the tissue buffer is exceeded, there is little mechanical factor of safety as represented by pulmonary ventilation and acute distress develops suddenly The normal subject, on the other hand, has a considerable pulmonary reserve and compensates for carbon-dioxid retention by increasing ventilation Consequently no sudden 'break' occurs but discomfort develops

gradually" These observations on the chemical changes in the blood, taken in conjunction with the decrease in the vital capacity of the lungs, throw an interesting light on the pathologic physiology of pulmonary emphysema, but in our experience the increase of carbon dioxid in the blood is only to be found in very advanced cases In the patient under consideration, for instance, the carbon dioxid of the blood was at a high normal level

When one examines the lungs of cases of pulmonary emphysema at autopsy, one is often somewhat disappointed to find that they do not conform to the preconceived picture Instead of the large, voluminous lungs that were expected, they may be found to be practically normal in gross appearance, and to be collapsed It is rather unusual to find the classical gross anatomic picture of emphysema, except in the very advanced cases For us, as clinicians, therefore, pulmonary emphysema is to be regarded less as an anatomic entity than as a physiologic entity, in which there is an interference with the normal range of respiratory movement It is the "bellows" function of the lungs that is affected This function normally has a large "factor of safety," so that in times of stress, as with hard exercise, when a large pulmonary ventilation is needed to enable the gaseous exchange in the lungs to keep pace with the demands of the metabolism, the amount of aeration of the lungs can be increased many fold In pulmonary emphysema however, as is indicated by the low vital capacity, the extent to which the lungs can expand and collapse with inspiration and expiration is definitely limited

In considering the relation between the heart and lungs in pulmonary emphysema one further point must be mentioned A cardiac lesion may develop as a secondary result of the pulmonary lesion Hypertropy of the right ventricle and functional weakness of the right side of the heart may occur In rare instances some degree of sclerosis of the pulmonary artery may also be associated with emphysema

The causes of pulmonary emphysema still remain somewhat obscure Occasionally one sees cases in which the emphysema

is apparently due to excessive expiration, as in glass-blowers and players of wind instruments, but much the most common factors seem to be asthma, with its prolonged expiration due to the spastic contraction of small bronchi, and recurrent infections Multiple attacks of acute bronchitis, or chronic bronchitis with acute exacerbations and long-continued low-grade infection of the bronchi between the attacks, account for most instances of emphysema We have recently observed a number of patients with marked emphysema who gave a history of influenza during the epidemic of 1918, and who have had prolonged attacks of bronchitis almost every winter since that time

Chronic pulmonary emphysema is thus a condition that must be seriously considered in certain patients in whom the presenting symptom is dyspnea on exertion Unfortunately, from the point of view of diagnosis it is most commonly met with in persons at an age when myocardial weakness might well be expected and it is very frequently met with in association with evident myocardial failure In the latter the cardiac condition is of course of the greater clinical importance, but in occasional patients the emphysema occurs alone or as the predominant feature It may be an extremely difficult task to differentiate in any given case the extent which the cardiac and pulmonary factors contribute to the production of the dyspnea No definite rule for such a differentiation can be laid down One must depend on a careful history and physical examination, particularly as these throw light on the presence of other evidences of heart disease, and in many cases only repeated observations over a considerable period of time will enable one to differentiate between the significance of the two conditions

The treatment of pulmonary emphysema is, at best unsatisfactory Various respiratory exercises have been devised with the aim of increasing the expiratory phase of respiration so that the volume of residual air may be reduced and the lung brought back to its normal condition, but they require prolonged and conscientious use Hofbauer,[3] in his book on "Atmungs-Pathologie und Therapie," has described one such

method that is interesting and ingenious In most cases, however, one must rely largely on prophylactic measures, such as the proper treatment of asthma and the prevention of recurrent attacks of infection of the bronchi

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CLINIC OF DR CHANNING FROTHINGHAM

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THE PROBLEM OF RHEUMATISM

IT IS interesting to check up from time to time on the work which has been done on an individual medical problem In some instances it will be found that real advance has been made, while in others, although a great deal of work has been done and many claims put forward, very little real advance has occurred It is especially important in those conditions about which much has been written to review the various claims every so often, in order to form a definite opinion as to just what the real situation is in regard to a particular disease From such a review the practising physician may hope to be able to form a clear mental picture of just what is really known about a certain disease and just what is the best method of procedure in such a case

Rheumatism comes in that group of diseases concerning which there has been a great deal of study and very much writing The fact, however, that there is such a divergence of opinion in regard to the exact nature of the disease and in regard to the methods of handling it raises the question as to whether there has been very much real advance on this subject in recent years For, if any one of the various procedures was superior to the others in the treatment of this condition, there would be more universal adoption of this method and more success in the results of treatment

It is important to have a clear conception of just what one means by rheumatism, as the term is often loosely applied to a variety of conditions in addition to diseases of the joints In this lecture I shall mean by rheumatism chronic disease of the

joints, excluding such specific conditions as gout, gonorrheal arthritis, and Charcot's joint One should realize that it has not as yet been established whether rheumatism or chronic arthritis is an individual disease, or represents a variety of abnormal conditions which produce lesions in the joints The clinical picture and the pathologic findings in different cases of chronic arthritis are quite varied and the question may well be raised whether one type of joint lesions may be due to one etiologic factor, while another type may be due to some other disturbance It is also conceivable that different etiologic factors might produce a similar lesion in the joints

At the present time our knowledge of the etiology of chronic arthritis may be summed up in the single word, unknown There are several theories in regard to these joint disturbances The one which is perhaps the most generally supported at present is that they are the result of infection Opinion is divided in regard to whether or not the organisms are actually present in the vicinity of the joints or produce their effect upon them by means of toxins Up to the present time no organisms have been isolated from the joints themselves or the surrounding tissues Another theory is that chronic arthritis is a metabolic disturbance If it is a metabolic disturbance it may be the result of some abnormality of the glands of internal secretion, some peculiar response of the individual to ordinary foodstuff, or some disturbance in the acid base equilibrium of the body Some workers feel that trauma is a factor in the disturbance to the joint surfaces It has been suggested that in some way anaphylactic phenomena may have some relation to the joint changes

The diagnosis of the condition is usually quite simple, for, as a rule, the patient comes to you with the definite complaint of rheumatism, and justly so, because there is often definite deformity and limitation of motion in the joints in addition to pain and stiffness on motion It is important for the practitioner to realize that at the beginning of the process there may be no deformity or limitation of motion and the only evidence may be pain in the vicinity of the joints and some stiffness

upon motion until the joints have become limber Slight swelling about the joints may appear quite early in the course of the disease Usually more than one joint is involved, although the patient's attention may be directed to just one joint because symptoms from it are more pronounced In the severer cases practically all the joints of the body may be involved

Except for the changes in the joints physical examination of the patient may show nothing of importance In some instances especially if the disease is active there may be a mild elevation of the temperature In the pronounced cases the patient may show the strain of the disease by undernourishment and secondary anemia Examination of the heart may show murmurs, which apparently develop during the course of some types of chronic arthritis This is of interest, because usually valvular heart disease is supposed to be associated with acute articular rheumatism, which is apparently quite a different disease This fact again raises the question of whether one type of chronic arthritis, at least, may not be a more chronic form of acute articular rheumatism In addition to the periarticular changes there is a certain amount of muscular atrophy, varying with the amount of limitation of motion in the different joints It has been suggested that in some types of chronic arthritis the body fluids, such as the saliva, sweat and urine, may show a higher degree of acidity than normal The usual clinical pathologic studies in these cases are, as a rule, unimportant In the early stages of the disease the x-ray pictures may not show any appreciable abnormality

Although the disease is usually diagnosed without difficulty there are certain conditions with which it may be confused It is important to separate rheumatism from these other conditions, as the type of treatment varies in the different diseases Gout often presents a joint picture which suggests chronic arthritis, but it should be differentiated by finding tophi, that is, deposits of uric acid crystals on the cartilage of the ear, by the appearance of the bones in the x-ray pictures, and by an increase of the uric acid in the blood Various painful and spastic conditions of the muscles, often spoken of as muscular rheumatism, may simulate a

chronic arthritis These usually can be separated by the absence of any deformity in the joint, and by the distribution of the spasm and tenderness of the muscles to just one single muscle or group of muscles These muscular spasms are also more temporary than the joint changes Closely identified with these muscular disturbances which, if occurring in the back, are frequently spoken of as lumbago are the symptoms which are supposed to be due to strain upon the sacro-iliac joints Tenderness over these joints, without involvement of other joints, differentiates this from chronic arthritis Bursitis must be separated from chronic arthritis, especially bursitis in the region of the shoulder-joint In bursitis the disturbance is usually limited to the region of only one joint, while in chronic arthritis, as has been mentioned, it is unusual for the process to be limited to just one joint Furthermore, in cases with bursitis the pain and limitation of motion is usually only in certain directions, while in arthritis it is apt to be painful upon any motion of an actively involved joint Also, in bursitis there may be tenderness on pressure in the region of the bursa Neuritis may produce a picture suggesting chronic arthritis, especially if the process is diffuse In neuritis there is not so much deformity of the joints, but more swelling and induration of the soft tissues The pain is also more independent of motion The joint disturbances due to some specific organism such as the gonococcus must, of course, be eliminated Gonorrheal arthritis is generally associated with some remains of acute or chronic infection with the gonococcus along the genital tract It also usually presents considerable swelling of the soft parts about the joints involved In cases with the Charcot joint other evidence of luetic disease of the central nervous system should be apparent

The treatment of rheumatism is a subject about which a great deal has been written and many different procedures recommended The fact that at the present time there is no universally accepted plan for the treatment of chronic arthritis is the best evidence that no really successful form of treatment has as yet been found As there are, however, so many different procedures recommended it is important to form a definite

plan for treatment in your mind for the individual case It is especially important in any disease in which the treatment is going to extend over a considerable period of time to have a definite program in mind in order to keep the patient from drifting aimlessly in his search for help Before outlining what seems to be the best line of procedure in the handling of a case of chronic arthritis the different methods of treatment that have been recommended will be discussed

The method of treatment suggested depends to a great measure upon what one's feelings are in regard to the etiology of the disease It is interesting, however, to note that in most instances the different workers on the subject are apt to recommend, in addition to their own particular method of treatment, at least some application of the methods of treatment outlined by other workers This, of course, is just a confession that they are not entirely satisfied with the particular method of procedure which they have advocated based upon their theories in regard to the etiology of the disease

At the present time the elimination of any possible focus of infection is receiving perhaps more attention than any other form of treatment If one is going to look for foci of infection it is important to have a clear conception of just what should be done It frequently happens that one meets a case of chronic arthritis in which the foci of infection have been thought of and perhaps one or more found and removed, but yet the whole question not studied in a comprehensive manner The more obvious foci of infection, such as chronic discharging ears pus in the urine or old discharging wounds from the bones, are not usually overlooked The various possibilities of so-called hidden foci of infection, however are often not systematically studied and, of course, if one is going to look for hidden foci of infection at all one should examine for all of the possibilities This means that a study should be made of the teeth, the accessory sinuses, the tonsils, the gall-bladder, possibly the appendix, the pelvic organs in the female the prostate and seminal vesicles in the male, and the intestinal tract It is also important to have a clear concept of just what it is necessary to do in examining

these various parts of the body in order to have a satisfactory examination with a minimum of expense for the patient Teeth must be examined by inspection in order to look for pyorrhea and also by x-ray study in order to find out what is going on at their roots, unless one is convinced that all the teeth are alive, in which case it is very unlikely that there are any blind abscesses about the roots An x-ray picture should be taken of the sinuses and they may be considered free from disease if the x-ray picture shows no clouding If, however, the x-ray picture presents a clouding further studies of the sinuses must be made by means of transillumination and inspection of their outlets The tonsils should be studied from the point of view of their action, namely, whether they are apt to become infected, also by inspection, and by palpation of the glands which drain the tonsils Unfortunately, there may be in the tonsils in certain cases some inflammatory reaction which is not obvious from inspection and which does not produce much, if any, local trouble Therefore, it is possible that chronic focus of infection may exist in the tonsils which cannot be ruled out by our present methods of examination It is probable, however, that infection is not often hidden away in the tonsils without giving some hint of its presence It must also be remembered that the surgeon may confuse the mixture of tissue juices, blood, desquamated epithelium, saliva, and secretions in the crypts of the tonsil with actual inflammatory lesions There is some question as to whether this material in the crypts of the tonsil can be looked upon as a focus of infection

In determining whether there is a focus of infection in the gall-bladder one must rely upon the story which the patient gives of attacks suggesting gall-bladder disease or stone in the gall-bladder Of course, obvious disease of the gall-bladder can be readily detected If there is evidence of a stone, it is a reasonable assumption that there is some chronic infection in addition The x-ray may be of some value in deciding the presence or absence of gall-stones The so-called Lyons-Meltzer method of examining the gall-bladder is in use in some clinics and quite favorable claims have been made in regard to the

diagnostic value of this procedure for demonstrating chronic inflammation in the gall-bladder This test has not been universally adopted for this purpose

The question of a hidden focus of infection in the appendix is one which is open to dispute, because, although it is generally conceded that the appendix may be the site of repeated attacks of acute infection, there is considerable doubt in the minds of many whether the appendix continues to remain in a state of chronic inflammation If the appendix is looked upon as a possible source of infection the decision in regard to the condition of the appendix can only be made from the history

The chronic inflammation in the pelvic organs in the female or in the prostate and seminal vesicles in the male should be sought for by digital examination

The possibility of absorption from the intestinal tract is one which always must exist, and therefore it cannot be ruled out as a possible focus of infection There is no way to eliminate bacteria from the gastro-intestinal tract and about all that can be done is to study the motility of the gastro-intestinal tract by x-rays or other means in order to see if the movements through the intestinal canal in an individual are particularly sluggish There is, however, no proof that simply because material moves through the gastro-intestinal tract at a slow rate of speed there is necessarily any more absorption of toxic products than in a normal individual, although such a supposition is a reasonable one

If one is going to look for foci of infection, it is important that all of the procedures mentioned above should be carried out, so that no one focus will be overlooked If any foci of infection are found, they should all be eliminated It is not reasonable to just treat the more pronounced ones In addition to removing any focus of infection attempts have been made to make a culture from the focus and to follow up the removal of the focus with a course of vaccine therapy It has also been suggested to change the character of the intestinal flora by means of diet and the introduction into the alimentary tract of different strains of organisms

The treatment of chronic arthritis by dietary procedures is also receiving a great deal of attention at the present time Pemberton has been one of the most active in this line in recent years and he favors not only cutting down somewhat on the gross amount that an individual eats, but especially on the carbohydrate intake It is quite a common event to have an arthritic patient say that they can bring on an attack of pain in the joints by eating a large amount of some sort of food, and in my experience the food most often mentioned as causing discomfort is some form of candy, especially of the chocolate variety Other workers on arthritis advise the avoidance of acid foods Unfortunately, it is not always possible to decide from the taste of the food whether it contains more acid or base, and also it is not known what effect these various acids in the food have upon the different body secretions, for it has been established that certain foods which are quite acid in their taste may contain a type of acid which is burned up in the body and excreted through the lungs, and still these foods may contain a considerable amount of base which will be excreted through the kidneys, so that they actually make the urine more alkaline Very little is known about the effect of the different kinds of food-stuff upon the sweat, saliva, and other body fluids Therefore, it is rather difficult at the present time, with our limited knowledge, to make any definite rules in regard to arranging a diet in order to avoid an increase of acidity

As it has been suggested that arthritis may, in some way, be an anaphylactic phenomena, associated with certain food-stuffs, some workers have studied the reaction of the patient's skin toward the proteins of various foods in order to see if the patient is sensitive, with the idea of avoiding in the diet any food-stuff to which the patient is sensitive

In regard to drug therapy, it should be admitted that there is no medicine which will have any effect upon the course of a chronic arthritis On the other hand, a variety of medicines are of benefit in relieving temporarily the symptoms Prominent among these are the salicylates The salicylates are recommended in various forms and different workers have enthusiasm

for different preparations The beneficial action, however, is no doubt due to the salicylates and it probably makes very little difference in what method the salicylate is given Glandular extracts have been mentioned with enthusiasm by some, but at the present time are receiving very little attention as a therapeutic agent of value in chronic arthritis The thymus and thyroid preparations have been the ones which have received the most attention

The treatment of chronic arthritis by the reaction to foreign protein has also been recommended and for this purpose typhoid vaccine has been given intravenously That this method of treatment has not been generally adopted is perhaps the best argument against its value Another reason which should make one feel some doubt in regard to its value is the fact that the use of typhoid vaccine intravenously has also been strongly recommended for the treatment of pneumonia and pernicious anemia

Orthopedic measures are of benefit in chronic arthritis These consist of rest for the diseased part, heat applied to the joints by various baking methods, sweating in order to increase elimination from the body as a whole, and massage around the joints with certain passive motions These various orthopedic measures are often successful in lessening the pain in the affected joints and improving the motion

It is quite obvious that all these varied procedures cannot be of specific value in the treatment of chronic arthritis It is important in handling such a case not to burden the patient with too extensive a course of treatment, especially if it may be doubtful of value Therefore it is wise to have some definite program to follow in the study and treatment for the patient with chronic arthritis With our present knowledge in regard to this disease the patient should be carefully studied for any foci of infection, and if any exist they should be eliminated. If no foci of infection are found, the question of arbitrarily removing the tonsils should be considered on the chance that there may be hidden away in the tonsils a focus of infection which cannot be diagnosed Although this procedure is radical,

it must be remembered that if the chronic arthritis is severe the end-results may be very distressing, and therefore it is worth while to undertake a therapeutic procedure, the value of which is uncertain, on the chance that it may be of help If there are no foci of infection, or after removing them and the tonsils the process continues, the patient should then be turned over to an orthopedic surgeon for baking, massage, etc In addition, it is very important to keep up the patient's general health by a liberal diet and to keep elimination active through the skin, bowels, and kidneys

In regard to the prognosis of chronic arthritis, it must be remembered that it is probably a self-limited disease in which there is a tendency for the active process to quiet down Just how much permanent damage will be done to the joints before the process quiets down, one cannot predict, and therefore it is important to endeavor to check the process It is difficult to decide whether the cessation of the activity of the process in an individual comes as the result of the treatment instituted or the natural course of the disease

CLINIC OF DR REGINALD FITZ[1]

PETER BENT BRIGHAM HOSPITAL

CLINICAL PROBLEMS IN THE DIAGNOSIS AND TREATMENT OF DIABETES MELLITUS

I A Possible Case of Arteriosclerotic Glycosuria Unimproved by Diabetic Treatment.

II A Possible Case of Cerebral Glycosuria Unimproved by Diabetic Treatment

III A Possible Case of Renal Glycosuria Unimproved by Diabetic Treatment.

IV. A Possible Case of Diabetic Coma Unimproved by Diabetic Treatment.

INTRODUCTION

IT IS usually considered that diabetes mellitus is an easy disease to recognize During the last year, however, several cases of persistent glycosuria in which it was difficult to establish the correct diagnosis have entered the Brigham Hospital, and I notice that Dr Joslin in his last paper in the Oxford Loose Leaf System says that he, too, is seeing a constantly increasing number of doubtful diabetic cases These facts lead me to present to you in this clinic 4 cases of possible diabetes, illustrating certain difficulties in diagnosis and treatment The subject is timely and important because accurate diagnosis is essential for good results in treatment and because the use of so powerful a drug as insulin in improperly selected cases may prove injurious

Case I A Possible Case of Arteriosclerotic Glycosuria.— The first case is that of a man sixty-two years old, who entered the hospital for diabetic treatment with this history

[1] From the Medical Clinic of the Peter Bent Brigham Hospital, Boston

The family and past histories were unimportant The patient had been a fairly active man most of his life, serving as an attendant in a theater, where he did administrative rather than physical work Eighteen years ago he weighed 240 pounds, he considered his average weight 215 pounds, and at entry to the hospital he weighed about 170 pounds

About a year ago he began to have dyspnea on exertion and edema of the ankles He consulted a doctor for these symptoms and was told that he had 4 per cent of sugar in the urine He dieted somewhat without any great improvement, finally giving up work seven months ago because his shortness of breath was so marked He was referred to the hospital, not for his presenting symptoms, but for diabetic treatment

The essential features of the physical examination were as follows The patient was obviously dyspneic on exertion, although there were no signs of peripheral edema The heart was enlarged according to percussion and the x-ray The sounds were distant and of poor quality, with a rough systolic murmur heard over the entire precordium There was marked thickening and tortuosity of the peripheral vessels and evidence of retinal sclerosis in the eye-grounds The systolic blood-pressure was 170 mm and the diastolic pressure 102 mm The pulse was alternating in quality An electrocardiographic tracing showed curves characteristic of left ventricular preponderance, delayed auriculoventricular conduction time, premature auricular beats, and defective intraventricular conduction time Yet despite so much evidence of advanced myocardial disease, the liver was not engorged, there was but little pulmonary edema, and the vital capacity a few days after entry was 110 per cent

The urine contained a trace of sugar and of albumin There were numerous hyaline and granular casts in the sediment, but no blood or pus The phthalein excretion was 48 per cent, pointing to an adequate renal function, while the blood-sugar concentration was 0 18 per cent, suggesting a mild diabetes There was no anemia, the Wassermann reaction was negative, and a stool specimen was normal

On the whole, the patient evidently had arteriosclerosis and chronic myocarditis, probably, renal sclerosis with some nephritis, and glycosuria with hyperglycemia Did he have diabetes? Should he be treated as a diabetic?

The graphic chart of the treatment followed in this case over a period of six weeks shows at a glance the remarkably poor result obtained when the patient was treated as a diabetic (Fig 230)

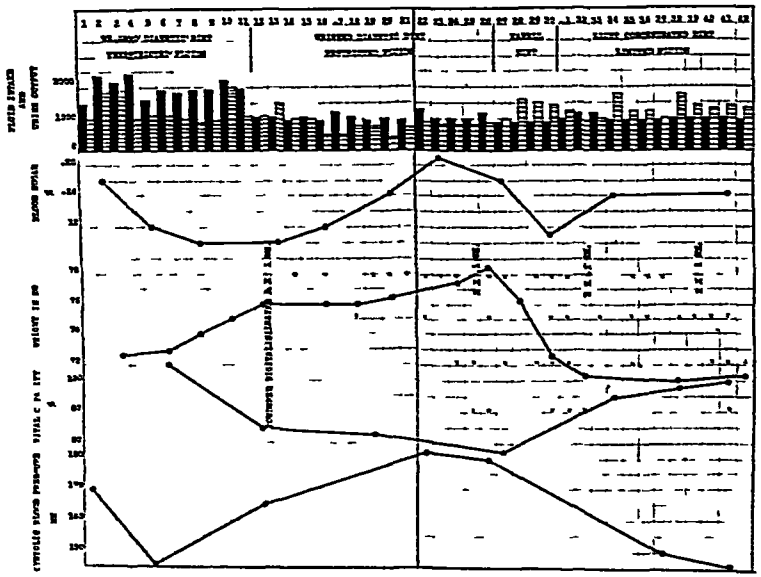

Fig 230

For the first eleven days the patient was given unlimited fluids and a strict diabetic diet made up as usual of fruit and green vegetables, broths, about 60 grams of protein in the form of meat and eggs, and varying amounts of fat The immediate effect of this treatment from a diabetic viewpoint was satisfactory The trace of urinary sugar disappeared, and the blood-sugar concentration fell to normal On the other hand, the patient began to gain weight, due to edema, the vital capacity fell, the blood-pressure after a slight initial fall began to rise, and the patient himself became increasingly dyspneic

For the next fifteen days the diet was kept unchanged,

although the fluid intake was restricted to less than 1500 c c per day and digitalis leaves were given in the dosage of 300 mg a day

During this period the patient grew steadily worse Even from a diabetic viewpoint, the tolerance did not increase, for while the urine remained sugar free yet the blood-sugar concentration rose, and from a general viewpoint the patient grew steadily sicker, since the edema and dyspnea increased, the vital capacity continued to fall, and the blood-pressure continued to rise

Thus at the end of twenty-six days of conscientious diabetic treatment we had a much sicker man to care for than at his entry to the hospital The blood-sugar was higher than at entry, there were 6 kg of edema to contend with, the vital capacity had fallen from 110 to 55 per cent, and the systolic blood-pressure had risen from its lowest point of 145 to 180 mm

At this time strict diabetic treatment was discontinued The patient was given Karell diet for four days instead of a diabetic diet This treatment was accompanied by an immediate fall in blood-sugar concentration, diuresis, loss in weight, gain in vital capacity, and fall in blood-pressure

Finally, for the last twelve days, the patient was given a light concentrated diet containing roughly about 150 gm of carbohydrate in bread, cereals, and 20 per cent vegetables, about 60 gm of protein, and an unmeasured amount of fat During this period the fluid intake was kept below 1500 c c each day and such traces of glycosuria as appeared were disregarded Under this management the blood-sugar concentration remained somewhat above normal, but not at a very high level, the urine output remained high, the edema disappeared, and with it the dyspnea which had previously been so uncomfortable, the vital capacity rose to normal, and the blood-pressure fell to 145 cm On the whole, there was no question but that the patient was better in almost every way when he was treated for heart disease than when he was treated for diabetes

This type of case is not uncommon There are a large number of elderly people with arteriosclerosis who may have a low sugar tolerance, a slight hyperglycemia, albumin and casts

in the urine, cardiac hypertrophy and hypertension, and either dyspnea on exertion or angina pectoris As a rule, these patients do not keep a progressive diabetes such as occurs in young people The diabetes, if it exists at all, is mild Treatment should be directed to the entire vascular disease rather than to the single phase of glycosuria A thorough and careful history and physical examination is necessary, so that due consideration can be given to all factors making up the picture The mere presence of glycosuria and hyperglycemia does not justify the diagnosis of diabetes or the establishment of too rigid diabetic treatment If the diabetes is treated at all, it should be handled gingerly and in a most conservative fashion

The use of insulin in this type of case should be mentioned I have followed the course of 2 such patients with insulin for a period of several months and am satisfied that both these cases have been more comfortable on 5 to 10 units a day, given in one dose, than they were without it This amount of insulin appeared to keep the blood-sugar level lower and to add a sense of well-being to the feelings, which was absent when the drug was not taken It is probably a good practice for this type of case to have a relatively normal blood-sugar figure, because such patients almost invariably have marked sclerosis of the vessels of the feet and are thus liable to develop gangrene, and because they often have corneal opacities which may go on to cataract formation While there is no positive evidence that hyperglycemia causes either gangrene or cataract, yet there is a pretty general impression that long-continued hyperglycemia exaggerates an elderly diabetic's known tendency to cataract, gangrene, or superficial skin infections Therefore, a relatively normal blood-sugar concentration is worth striving for, and certainly, if a small single daily injection of insulin makes the patient feel better, it is worth using

Case II A Possible Case of Cerebral Glycosuria.—The second case is that of a trained nurse forty-three years old who entered the hospital for diabetic treatment with this history

The family history showed that an uncle on the father's

side had diabetes at the time of his death, a brother was at one time refused life insurance because of diabetes, and a sister was supposed to have diabetes at the present time The patient had never been particularly strong, although she was always able to work effectively Her appendix had been removed sixteen years ago Five years ago her menopause was accelerated by x-ray treatments because of dysmenorrhea and undue physical symptoms During the war she worked in a war hospital and went through numerous air-raids, as a result of which she developed symptoms suggesting shell-shock For many years she had been liable to fairly frequent severe and prostrating sick headaches which would lay her up for two or three days at a time

The present illness began fourteen years ago when, while in training, she complained of "swelling of the legs" Because of this she had a medical examination and was found "to have sugar and albumin in the urine and a heart that was not very strong" At that time she weighed 108 pounds

During the last fourteen years she has dieted more or less, carefully avoiding sugar, cake, bread, and potatoes, and has been fairly comfortable In 1916 she consulted Dr F G Brigham, who has been kind enough to send me a summary of his findings I have charted the relevant data in order to illustrate the progress of the disease as clearly as possible

The Progress of an Atypical Case of Diabetes During a Period of Over Five Years

Date	Urine, sugar	Blood-pressure, mm	Weight in pounds	Blood sugar, per cent.
April, 1916	Trace	115	113½	
December, 1917	0		96	0 06
1918				
Seen eleven times	0–Trace		109¼	0 11–0 15
1919				
Seen four times	0–1 per cent		Curve of alimentary tolerance test following 72 gm of glucose Fasting, 0 09, 0 14 (one hour after test-meal), 0 11 (two hours after test-meal)	
April, 1920	0 3 per cent	160	119	0 13–0 15
May, 1921	0	160	128	0 21
December, 1921	0 1 per cent	165	142	0 33

From Dr Brigham's record it appears that from 1916 until 1921 no significant glycosuria developed, there was a progressive gain in weight and a progressive rise in blood-pressure, out of several blood-sugar determinations only two were notably abnormal, and a sugar tolerance test in 1919 did not result in a typical diabetic blood-sugar curve On the other hand, it may be significant that the blood-sugar concentration gradually tended to increase as the body weight increased, a sign pointing to an underlying true diabetes

The patient came to the Brigham Hospital in May, 1924 Until three months previously she had been going on as usual feeling well enough, holding her weight at about 140 pounds, dieting with discretion, but not taking her glycosuria too seriously About three months before her entry here she began to lose weight, to feel tired out all the time, to find difficulty in sleeping, and, in general, to appear to be failing for no apparent reason, despite what appeared to be a perfectly adequate diet.

The physical examination showed that the body weight was 120 pounds proving a definite recent weight loss The blood-pressure was 160 mm and the disk of the right eye-ground had slight but definite choking The urine contained a trace of sugar after a hearty breakfast, and the blood-sugar concentration was 0 12 per cent At that time an accurate diagnosis seemed impossible It was difficult to believe that the slight glycosuria in the absence of any typical diabetic symptoms was the cause of the loss of weight and sense of prostration The eye-ground changes suggested a possible cerebral tumor, but there were no neurologic signs by which localization of any growth was possible On the whole, there seemed nothing to do but wait developments

During the last six months until recently matters remained unchanged On several occasions blood-sugar determinations were made which varied between 0 12 to 0 16 per cent The urine never showed more than a trace of sugar despite considerable variation in diet The body weight remained constant. Sometimes the patient felt fairly well, at other times very tired and depressed

A few days ago the patient suddenly became very weak and stuporous Examinations now showed bilateral partial ptosis, the right pupil was larger than the left, there was bilateral nystagmus, a positive Romberg sign, edema and slight choking of both optic nerve disks, and an exaggeration of the deep reflexes in both arms, with diminution of the deep reflexes in both legs The blood-pressure was 130 systolic and 80 diastolic The urine was sugar and albumin free The patient was admitted to the hospital on Dr Cushing's service, where Dr Cushing made the clinical diagnosis of probable cerebral tumor

In brief, here we have a patient with glycosuria at the age of thirty, persisting for fourteen years, without any of the cardinal symptoms of diabetes, with severe repeated headaches, finally accompanied by choked disks and neurologic signs of organic disease of the central nervous system Has she diabetes? Should she be treated as a diabetic?

I have presented this case to bring out once more the importance of the careful clinical study of all cases of diabetes Personally, I am inclined to think that this patient is not suffering from diabetes mellitus, but that the glycosuria is of cerebral origin, due in some fashion to intracranial pressure from a slowly growing tumor Time will tell whether or not this opinion is correct In any event it is evident from the patient's story that she felt worse when she tried to diet too strictly and when she was much underweight I believe that had she been advised to diet more rigorously or to take insulin without careful study on the strength of a persistent mild glycosuria that she might have been made more uncomfortable than ever

Case III.—A Possible Case of Renal Glycosuria—The third case is that of a medical student twenty-eight years old, who came to the hospital complaining of "glycosuria"

The family history was not remarkable In the past the patient had always been well except for an appendectomy for acute appendicitis fifteen years ago and for an operation for the removal of a stone from the left ureter two years ago

The present illness began four months ago when the patient tested his urine and found that it contained sugar At that time he weighed 150 pounds As a result of this urinalysis he naturally became disturbed and began to treat himself for diabetes by pretty rigorous dietetic restrictions He found that sugar appeared intermittently in the urine in small amounts, and apparently bore some relationship to the amount of food eaten There was never any excessive appetite or polyuria and no great loss of strength, though by curtailment of diet there had been a progressive weight loss of about 10 pounds

Routine physical examination was negative There was no anemia The Wassermann reaction was negative A twenty-four-hour specimen of urine was sugar free and the blood-sugar concentration in the middle of the afternoon was 0 09 per cent. Has the patient diabetes? Should he be treated as a diabetic?

In order to make a diagnosis in this case it seemed first necessary to obtain an idea as to what the sugar tolerance was With this idea in mind the patient was told to weigh and record all food eaten for three meals and to return with a complete twenty-four-hour specimen of urine and his diet list

On analysis, the diet was found to contain approximately 40 grams of carbohydrate, 90 grams of protein, and 140 grams of fat, yielding about 1780 calories It may be of interest to record in what form this amount of food was taken

A TYPICAL DIABETIC DIET

Breakfast 1 egg
5 gm. butter
15 gm. oatmeal
60 gm. 35 per cent cream

Dinner 2 eggs
30 gm. bacon
10 gm. butter
150 gm spinach
50 gm. tomatoes
30 gm. orange
30 gm 35 per cent cream.

Supper 60 gm. grapefruit
200 gm. steak.
5 gm. butter
50 gm. 35 per cent cream.
100 gm. tomatoes
60 gm. lettuce

Since the urine was sugar free, and since the patient said that the diet was sufficiently satisfying to his appetite, it seemed best to use this amount of food as a basis from which to build in determining tolerance For the following twenty-four hours the patient was given this diet with three shredded wheat biscuits added The urine was still sugar free Then six slices of bread were added to the shredded wheat and the diet The twenty-four-hour urine gave a suggestive reaction with Benedict's solution Then 6 cubes of sugar were added to the bread, shredded wheat, and the diet The twenty-four-hour urine now contained a trace of sugar, however, the blood-sugar concentration an hour after dinner was only 0 14 per cent Finally, an alimentary sugar tolerance test was performed The patient was given 100 gm of glucose in 500 c c of water in the morning on a fasting stomach, blood-sugar determinations being made before the glucose was ingested, a half hour later, an hour later, two hours, and three hours later Specimens of urine were obtained at the same time as the blood samples were withdrawn and were tested for sugar The stomach was emptied by a small tube at the end of the observation in order to make certain that no sugar was being retained in the stomach The result of this test is tabulated

An Alimentary Sugar Tolerance Test

Time	Urine sugar	Blood sugar per cent.
7 00 A M	Trace	0 08
	100 gm of glucose ingested	
7 30 A M	Trace	0 11
8 00 A M	Trace	0 07
9 00 A M	Trace	0 06
10 00 A M	0	0 06
	Gastric residue sugar free	

On the whole, it appears that the glycosuria bore no particular relation to the degree of glycemia, the renal threshold for glucose was low because a trace of sugar was excreted when the blood-sugar concentration was between 0 06 to 0 07 per cent , 100 gm of absorbed glucose did not produce any hyperglycemia, there was no evidence from the result of the

test to justify the diagnosis of diabetes mellitus, and the blood- and urine-sugar curves appeared fairly typical of so-called renal glycosuria

The question arose as to what to advise by way of treatment My own experience with renal glycosuria is very limited and I have a wholesome fear of even the intermittent presence of sugar in the urine of a young person Therefore, I have advised this patient to report at monthly intervals during the year, to eat a liberal enough diet to almost satisfy his appetite, but to avoid cake, candy, sugar, pastry, and too much of the high carbohydrate foods like bread and potato, and, above all, to avoid any great gain in weight

The patient has reported twice since the sugar-tolerance test was made Both times he was feeling well, the urine contained a trace of sugar, and the blood-sugar concentration was less than 0 10 per cent The last time I saw him his weight was 147 pounds

This case is presented to illustrate once more the difficulties in diagnosis of certain cases of glycosuria and the harmful effect of treatment in improperly selected cases This patient made the diagnosis of diabetes in his own case on insufficient evidence and treated himself so rigidly that he rapidly lost considerable weight Such rigid treatment was unnecessary in view of the sugar-tolerance test Had the patient been given insulin from the outset, because of the glycosuria, without other manifestations of diabetes, he might have been seriously injured Remember, therefore, that a persistent glycosuria must always be taken seriously, but that rigid diet and insulin should not be used unless the diagnosis of diabetes mellitus can be proved

Case IV A Possible Case of Diabetic Coma—The fourth case is that of a woman sixty-one years old, who entered the hospital in so nearly a comatose condition that only the following rather fragmentary history could be obtained

The patient's mother died of diabetes and a living sister was a diabetic

The patient had been well all her life and able to do ordinary housework Two years ago she weighed 160 pounds, during the last six months she had lost 30 pounds in weight

Her present illness began two years ago when sugar was found in the urine At this time she dieted and kept sugar free During the last few months, however, she had abandoned her diet and had gradually lost weight and strength, and had complained of increasing hunger, thirst, and polyuria

Two months ago she became so debilitated that she could no longer do her housework Three days ago she took to her bed from weakness Twenty-four hours ago she "went out of her head," and twelve hours ago she became unconscious and comatose

Physical examination was not particularly remarkable The heart, lungs, and abdomen seemed negative The systolic blood-pressure was 115, with a diastolic pressure of 70 The temperature was subnormal at entry, the pulse-rate slightly elevated The hemoglobin concentration was 86 per cent, the red count 4,850,000, and the white count 21,200 The urine had 1 5 per cent of sugar and a strongly positive diacetic acid test, it contained a trace of albumin and numerous casts The blood-sugar concentration was 0 51 per cent and the alkali reserve 18 volumes per cent On the whole, the patient seemed to present the clinical picture of severe diabetic acidosis and accordingly was given insulin and routine diabetic coma treatment Everything seemed to be progressing satisfactorily for eighteen hours after entry, when suddenly the patient died Necropsy revealed, as cause of death, infarct of the heart with rupture of the left ventricle and hemopericardium

In the Peter Bent Brigham Hospital there have been a few cases in which insulin has apparently been ineffectual These cases in a general way have been of two types On the one hand, there have been a certain number of fat diabetics in whom insulin subcutaneously administered has not appeared to have its usual effect This lack of insulin effect may have been in part due to the fact that a large amount of subcutaneous adipose tissue in some way interfered with the absorption of insulin,

or that insulin in being absorbed slowly was transformed into some inert substance There is no proof for this impression I believe, however, that stout people, if they urgently need insulin, should receive the drug intravenously during the period of emergency

On the other hand, there have been several fatal cases with acidosis or coma in which insulin has failed to accomplish anything In many of these cases blood and urine analyses have shown that insulin was pharmacologically active and the necropsy has shown that some complication was the direct cause of death Dr Christian has very aptly termed such cases "the fatal cases of diabetes apparently cured in the laboratory" The last case is an example of this group Here insulin seemed to be benefiting the patient as judged by laboratory tests, because the acetone body excretion ceased, the percentage of sugar in the urine diminished, and the blood-sugar concentration[1] fell Yet despite such encouraging laboratory findings the patient died

It is a most important matter to obtain careful data upon the possible ineffectiveness of insulin under various conditions One method of obtaining such data is by carefully controlled clinical studies Another method is by pathologic examination of all fatal cases More fundamental knowledge of the pathology of diabetes and its complications is as necessary now as it has ever been, and future advances in our knowledge of this disease will continue to be made by careful correlation of clinical facts observed before death with the findings obtained postmortem Therefore, I urge all of you to obtain postmortem examinations on your fatal diabetic cases and to be dissatisfied with clinical diagnosis alone Remember this case as an example Without a necropsy it would probably have been considered as a somewhat atypical case of diabetic acidosis unimproved by insulin treatment As a result of the necropsy

[1] A sugar determination was made on a sample of the heart's blood removed seven hours postmortem. The reading was 0 12 per cent How much a factor postmortem glycolysis may have been in lowering the blood-sugar concentration is uncertain

we know that the patient had an incurable form of heart trouble, and that the diabetic acidosis was but a complicating factor

CONCLUSION

In this clinic I have presented 4 cases to illustrate that the diagnosis of diabetes mellitus may be difficult The mere presence of glycosuria no longer justifies the clinical diagnosis of diabetes Radical diabetic treatment, especially with insulin, may do a great deal of harm to improperly selected cases Certain cases appear refractory to insulin Pathologic studies of diabetes are as necessary now as they have ever been

CLINIC OF DR CYRUS C STURGIS

THE PETER BENT BRIGHAM HOSPITAL

CASES OF EXOPHTHALMIC GOITER ILLUSTRATING THE SPONTANEOUS COURSE OF THE DISEASE AND THE EFFECT OF VARIOUS TYPES OF TREATMENT

DURING the past ten years many advances have been made in the clinical management of patients with exophthalmic goiter, one of the most notable being a greater ability to state more correctly if the patient has or has not hyperthyroidism This results from an increased knowledge concerning the characteristic clinical picture and the great assistance which is derived from a study of the basal metabolism While it appears to be a uniform opinion that the diagnosis of hyperthyroidism is now accomplished with great accuracy, provided the patient remains under observation a sufficient length of time, the conclusions regarding our present-day treatment are less satisfactory, as there is not complete agreement concerning this matter Within the past few years, however, the conclusion has been among the majority of observers that surgery offers the greatest relief to the largest number of the patients in the shortest time There are at present at least two reasons why it is impossible to state definitely the efficiency of the various types of treatment offered as a cure of hyperthyroidism The first is that there are no observations in a large series of patients in whom the spontaneous course of the disease has been carefully studied over a period of several years The most valuable data bearing on this phase of the disease is the study of Kessel, Lieb, and Lande,[1] who found that 82 per cent of a series of 51 patients were able to return to their former social and economic activities, most of them within six months, al-

though they received no other treatment than rest, psychotherapy, removal of foci of infection, and syrup of ferrous iodid While these patients cannot be regarded as untreated, yet these observers deserve a great deal of credit for emphasizing that with comparatively simple treatment a large percentage of these patients show at least striking temporary improvement The second objection to a satisfactory deduction concerning the treatment of this condition is the lack of careful observations, including the basal metabolism, over a long period following different types of therapy While it is true, for instance, that there is usually a marked drop in the basal metabolism and a great improvement in the general condition of the patient immediately following subtotal thyroidectomy, yet no large number of convincing observations are available which tell us the condition of these patients five, six, or even ten years later, although we know that a certain proportion of them remain perfectly well These objections, of course, apply equally well to the conclusions concerning all forms of treatment which are used in hyperthyroidism

The following cases seemed worthy of a report, as they illustrate some important facts concerning the spontaneous course, the treatment, and complications of exophthalmic goiter, which are of practical importance in the management and care of these patients

Case I Mild Hyperthyroidism Terminating Spontaneously—A married shoe-worker, aged fifty-four, entered the hospital May 29, 1918, complaining of "weakness and loss of weight" His family history and past history were irrelevant

Past Illness—One year before admission the patient had a minor operation on his foot Following this he developed considerable weakness, but after a rest of six weeks returned to his work He found this too strenuous and after several months was obliged to give up on account of nervousness, weakness, and a loss in body weight of 41 pounds During this time he became very restless and irritable and did not sleep well He was troubled with moderate dyspnea on exertion There had

been no change in the appearance of his eyes or in the size of his neck Recently he had drunk more water than usually, often taking as much as 2 to 3 glasses per hour Nocturia had been present two to three times almost every night for several years

Physical examination showed a rather nervous individual who gave evidence of recent loss of weight The eyes had a slight staring appearance, but there was no definite exophthalmos The thyroid was not enlarged although the isthmus was readily palpable There was a definite brownish pigmentation in the roof of the mouth face, and over the body A moderate fine tremor of the extended fingers was present The left border of cardiac dulness was just outside the nipple line, and roentgenogram of the heart showed slight enlargement Electrocardiogram showed left ventricular preponderance The resting pulse-rate was 89 per minute, while the rate recorded on the ward reached as high as 110 per minute The basal metabolism was +42 Body weight was 60 kg without clothing The adrenalin test was positive A twenty-four-hour sample of urine contained a very slight trace of sugar

The nervousness, loss of 41 pounds in body weight despite a good appetite, pigmentation, tachycardia, the slight glycosuria, tremor of the extended fingers, staring expression of the eyes, and elevated metabolism suggested very strongly the diagnosis of hyperthyroidism The patient was advised to rest completely and report to the Out-door Department for observation No further word was heard concerning his condition until November 17 1919, approximately eighteen months after leaving the hospital He then appeared with the story that he had been doing light work at home during that interval Within six months after leaving the hospital he had attained his normal body weight, the nervousness disappeared, and he was no longer troubled with ease of fatigue or other symptoms A few weeks before returning to the hospital he had been able to start work in an office His only reason for presenting himself was to show how much he had improved Physical examination at this time was essentially normal, except a slight enlargement of the

heart which had been previously noted He appeared well nourished and no longer had the characteristic demeanor which was present a year and a half before His resting pulse was 62 per minute, and his body weight, without clothing, was 69 8 kg , a gain of 9 8 kg , or 21 6 pounds The basal metabolism at this time was −4 per cent The adrenalin reaction was doubtful, whereas previously it had been positive

No further information was available concerning this patient until October 7, 1924, when he returned for observation in response to a letter He stated that he had been perfectly well and considered himself entirely normal He had not been troubled with palpitation, nervousness, dyspnea, excessive perspiration, or increased warmth Physical examination showed a well-nourished, healthy appearing, middle-aged man The only abnormality revealed was the slight staring appearance of the eyes which had been noted before The basal metabolism was +7, the resting pulse-rate 56 per minute, and body weight 72 2 kilograms

In summary, this patient had hyperthyroidism over an interval of one and a half years About five years ago all of his symptoms disappeared without treatment, and he has had no evidence of the disease since then This case, to be more convincing, should have shown the more conspicuous signs of exophthalmic goiter, such as definite exophthalmos and an enlarged thyroid gland There seems to be no question about the diagnosis, however, and patients with a similar spontaneous course, in whom the diagnosis has been obvious, have been observed This indicates, therefore, that all the symptoms of this condition may completely disappear spontaneously for a considerable period of time There is a possibility that a second wave of the disease may occur in this individual in the future or there may never be any further evidence of the condition The frequency of spontaneous remissions is not known, but it seems very unwise to withhold all treatment, in hopes that such may occur A spontaneous arrest or cure, as shown by this patient, illustrates the difficulty experienced in judging the effects of various types of therapy

Case II Six Exacerbations of Exophthalmic Goiter in Fifteen Years, With Death From Chronic Cardiac Disease — P M E, aged forty-five, entered the hospital on September 29, 1919, complaining of "shortness of breath and palpitation" For the previous six months the patient had been a salesman in the vicinity of Boston, while for twenty years prior to this time he had served as a manager of various hotels He had been jaundiced about eighteen months before admission, and this symptom in association with acute abdominal pain, led to a diagnosis of cholelithiasis At the age of twenty-one, twenty-four years ago, he had developed a chancre which had disappeared with very little treatment

Present Illness —In 1904, fifteen years before admission, the patient developed nervousness and weakness, his body weight decreased in two months from 185 to 145 pounds, and it was observed that his eyes were becoming more prominent He was sent to a hospital and put to bed for four weeks At this time the patient stated that potassium iodid was administered (probably on account of his syphilitic infection) Following a vacation of four months after discharge from the hospital, all of the symptoms subsided, with the exception of the exophthalmos, and the patient resumed his work as the manager of a hotel in New York, where he remained for a period of three years During this time he continued to have perfect health During 1907, about twelve years before admission, he had a recurrence of all of his symptoms which kept him away from his work for six months, although he was not confined to bed during this time He then resumed his occupation and was apparently in good health until 1910, when he had a third recurrence of all his symptoms He went to a hospital and during a routine physical examination was found to have an incidental bladder condition for which an operation was performed The exact nature of this was unknown, although it was probably for the removal of a vesicle calculus Following a rest of three months he was able to resume his work as a hotel manager In 1912 there was a fourth recurrence of symptoms such as nervousness, palpitation, dypsnea, and loss of

weight At this time he was confined to bed for four weeks in a hospital and remained at home for two months recuperating Following this he apparently had very good health until 1918, a year before admission, when his previous symptoms again appeared, which made it necessary to remain three weeks in a hospital, and two months resting at home He then changed his occupation to that of a salesman, which he considered less strenuous He kept at this work until May, 1919, which was just five months before admission At this time his dyspnea, palpitation, and nervousness became so marked that he was obliged to give up his occupation and came to the Out-door Department of the Peter Bent Brigham Hospital for treatment It was found that he had a positive Wassermann, and syphilitic treatment was administered in the form of potassium iodid

As his condition did not improve he was shortly after admitted to the hospital for treatment Physical examination showed marked exophthalmos, a symmetric, moderate enlargement of the thyroid gland, with a systolic thrill over the right superior thyroid artery The patient obviously had cardiac failure, which was evidenced by rather marked dyspnea on exertion, orthopnea, and an enlarged heart with an absolutely irregular rhythm The patient remained in the hospital for three days, when he left, against advice, as he stated it was essential for him to finish up some outside business He returned in about eight weeks in very much worse condition, as shown by marked dyspnea, a large pulse deficit, and striking edema of his lower extremities, penis, and scrotum After rest and the administration of a considerable amount of digitalis the patient's cardiac condition improved markedly and it was possible to obtain his basal metabolism for the first time This was found to be 21 per cent above normal He remained in the hospital fifty-one days, and after showing considerable transient improvement in his heart condition rather rapidly became worse Fluid developed in the left pleural cavity, a moderate edema of the lungs became apparent, and rather striking edema of the lower extremities appeared After his condition had remained unchanged for several days, he sud-

denly became very cyanotic and respirations abruptly ceased Autopsy held seven hours postmortem showed hyperplasia of the thyroid gland, hypertrophy and dilatation of the heart and myocardial necrosis

In summary, this patient was a man of forty-five who gave striking evidence of having had exophthalmic goiter over a period of fifteen years During this time he had received no treatment other than rest and an occasional course of potassium iodid which had been given on account of his syphilitic infection The characteristic symptoms appeared in waves averaging about three months, and occurred during 1904, 1907, 1910, 1912, 1916, 1919 On close questioning, he stated that following each attack his exophthalmos and goiter remained unchanged, but there was a tendency for him to have more dyspnea and palpitation as residual symptoms following each exacerbation of the disease When first observed in this hospital his difficulty was not with hyperthyroidism, as shown by the very slight elevation in the metabolism (+21), but with a very much damaged heart, which was the ultimate cause of his death, and was apparently the direct result of the exophthalmic goiter

This patient's history has been presented, as it emphasizes the following important facts concerning exophthalmic goiter

1 The natural course of the disease is often characterized by remissions

2 Although striking remissions may occur, yet there is a tendency to recurrence, and each exacerbation results in a certain amount of cardiac damage, which may cause the patient to become a chronic invalid and eventually end with death from heart failure

We rarely have an opportunity to observe the natural course of the disease over a long period in these patients in the present day, as they are treated in one way or another as soon as the diagnosis is established Plummer[2] has very correctly emphasized that as the disease tends to progress in waves of approximately three months' duration and as the patients are likely to present themselves to a physician during the rise or at the peak of the wave, improvement will follow at this time in

many patients as a result of the natural course of the disease and regardless of the type of treatment which is instituted The older clinicians, who had the opportunity of observing patients with exophthalmic goiter before surgery was so generally offered as a cure, recognized more clearly these remissions and relapses in untreated cases Trousseau [3] for instance, in 1861, says as follows, " paroxysms may return at long intervals only, of several months or several years, and may vary indefinitely as to their duration and gravity The disease may go on increasing for several months and then remain stationary for one or two years, paroxysms no longer show themselves, and the stage of decline then begins It rarely happens that the disease disappears completely, it merely recedes, and there always remains swelling and induration of the thyroid gland, with unusual prominence of the eye-balls.

The functions of the stomach and of the intestines become normal again, the temper ceases to be capricious, and the patient is able to resume his or her occupation "

The second point of importance in this patient's history is the effect of each wave of hyperthyroidism on the heart His cardiac symptoms following each attack became more marked and the heart damage was the ultimate cause of his death. Cardiac symptoms, such as palpitation and dyspnea, are part of the clinical picture of exophthalmic goiter, and early in the disease they do not usually represent serious injury to the heart muscle, but auricular fibrillation, often of a transient nature, has been observed even in patients whose symptoms of hyperthyroidism have been of relatively short duration The prevention of serious and permanent cardiac damage constitutes one of the strongest arguments in favor of the early removal of the major portion of the thyroid gland, and this is one condition wherein the cause of heart failure may be eliminated Had this patient been treated surgically, according to our modern methods, it is very probable that his cardiac disease would have been averted Therefore, although many patients with exophthalmic goiter may show intervals of improvement, although no treatment is given, the early surgical treatment of

the condition should be carried out to prevent serious cardiac complications

Case III Immediate and Striking Improvement in a Patient with Exophthalmic Goiter Following the Use of the Roentgen-ray—A married housewife, aged forty, was admitted on October 22, 1921, complaining of "nervousness and palpitation"

Family history was negative

Past History—The patient had always been well and strong, although she had always been somewhat nervous

Present Illness—The onset was eighteen months before entrance, when the patient began to suffer from palpitation, and this was followed very shortly by extreme nervousness and tremor of the hands Her weight decreased 20 pounds, although she characterized her appetite as "ravenous" She complained of feeling warm all of the time and perspired excessively Six months before admission she apparently had experienced a brief remission, as her condition improved and she gained somewhat in body weight This, however, was of short duration, for after two months all of her symptoms returned, and she suffered from insomnia and became very nervous, restless, and irritable About one week before admission her neck was observed to be enlarged, although she had not noticed any prominence of her eyes at any time On admission to the Out-door Department a diagnosis of hyperthyroidism was made, but as her condition was thought to be acute she was admitted to the medical service in order to prepare her for operation Physical examination showed an exceedingly restless and nervous, middle-aged woman There was slight exophthalmos and a definite lid-lag The skin was moist and the surface temperature was elevated The thyroid gland was moderately enlarged on both sides, but more markedly on the right. A distinct thrill was felt over the right lobe and a systolic bruit was heard over both lobes The left border of cardiac dulness measured 14 cm from the midsternal line, while the right border was at the sternal margin The heart action was rapid, but regular There was a definite fine tremor of the extended

fingers The patient's metabolism shortly after admission was found to be +37 It was decided to try the Roentgen ray as a therapeutic measure, and the striking results are shown in Table 1

TABLE 1

Date	Pulse per minute	Body weight kg	Metabolism per cent of normal (DuBois)	Activity
1921				
October 25	118	61 2	+37	Rest in bed
October 29	126	60 3	+51	
November 1	First Roentgen ray treatment			
November 21	Second Roentgen ray treatment			
December 12	Third Roentgen ray treatment			
December 27	86	59 0	+25	
1922				
January 6	Fourth Roentgen-ray treatment			At home doing light work
January 27	Fifth Roentgen-ray treatment			
February 10	68	60 8	−17	
February 21	72	61 2	− 6	
March 14	74	61 7	− 4	
April 13	68	64 4	−14	
June 20	68	67 1	−14	
October 20	74	68 0	−10	

Case III The patient was admitted to the hospital on October 22, 1921 Duration of symptoms eighteen months Five Roentgen-ray treatments were followed by a prompt drop in the metabolism to normal, where it remained during the period of observation

The course of the disease in this patient indicates that a complete recovery of at least one year's duration may follow Roentgen-ray treatments The exact value of the Roentgen ray in exophthalmic goiter has been in dispute within recent years In 1919 Means and Aub[4] concluded that "the chance of cure in exophthalmic goiter is as good with the Roentgen ray as with surgery, in groups of equal toxicity, and that being true, the former method is preferable, for the danger of a fatal outcome is less" In the past five years surgical methods of treatment have improved markedly and the group of observers at the Massachusetts General Hospital[5] now conclude that subtotal thyroidectomy offers the greatest possibility of cure in this condition They do feel that irradiation is of value, and

conclude that in a third of the cases there is no evidence of improvement, in the other two-thirds there is evidence of improvement, while in a minority there is a rapid and striking beneficial effect My own personal experience has been very similar to this, that is, in many patients there has been no improvement, in a moderate number there has been some improvement, which could not always with assurance be attributed to the Roentgen ray, and in a relatively small group there has been a prompt cure which has persisted for as long as they have been observed The group of patients who improved somewhat following treatment should be classed as failures, as a cure must be indicated by a permanent reduction of the basal metabolism to a point within normal limits Moderate improvement cannot by any means be considered a therapeutic triumph This patient, whose history has been given made a prompt recovery with a fall in the basal metabolism to −17 per cent in about two and a half months following five Roentgen-ray treatments, and she remained under observation for a year with a metabolism which remained within normal limits

This is a result which ordinarily would be considered as satisfactory if the improvement had followed surgery To be classed as a cure, however, the patient must be observed for a period of years, and in this particular instance, unfortunately, it has been impossible to obtain further data concerning her condition for more than one year after treatment The criticism may also be offered that the improvement in the patient's condition may be entirely due to a spontaneous remission This is not probable, as treatment was instituted when her condition was rather rapidly becoming worse In addition, other instances of striking benefit following irradiation have occurred in this hospital, and the improvement has been more marked than is ordinarily observed during the spontaneous course of the disease

I do not recommend the routine use of the Roentgen ray in the treatment of exophthalmic goiter, as the results from surgery are much better Not infrequently, however, a patient refuses operation or desires other treatment in the hope of avoiding

surgery It seems worth while, therefore, under such circumstances to offer Roentgen-ray therapy if the patient understands that a cure is entirely possible, but the chances are not great, and provided that the condition of the heart is such that an additional period of three months, during which time the treatments are given, will not result in serious cardiac injury The best routine to follow in the treatment is to give four exposures at intervals of three weeks The patient is then observed for six weeks following the last treatment The basal metabolism is determined at frequent intervals to prevent the possibility of overtreatment and a resultant myxedema If striking improvement does not follow four Roentgen ray exposures, little more can be expected of it, and further treatment of this nature should be discontinued

Case IV Recurrence of the Symptoms of Exophthalmic Goiter Eight Years after Partial Thyroidectomy, Treatment with Lugol's Solution Followed by a Second Resection of the Gland.—A E H, aged twenty-five, entered the hospital on October 8, 1915, complaining of a "rapid, nervous heart" He had always been strong and healthy with the exception of "swollen glands" of the neck, which had been removed seven years before admission, and an attack of abdominal pain which was followed by an appendectomy six years prior to entrance His occupation had been that of a carpenter, but he was obliged to give this up, as the work was too hard and he was troubled with dyspnea and palpitation More recently he had been working in a barber school

Present Illness—His illness began three months before coming to the hospital, at which time he noted moderate dyspnea and palpitation on exertion He became nervous, irritable, and easily excited His appetite had continued good, but his weight had decreased 14 pounds in the year prior to admission Physical examination showed moderate exophthalmos and a definite lid-lag There was a firm, moderate enlargement of the thyroid gland, slightly more on the left than the right A fine thrill could be felt below the lower border of the sternomas-

toid muscle on the right, and a loud continuous bruit was heard over this same area The heart borders measured $10\frac{1}{2}$ cm to the left and $2\frac{1}{2}$ cm to the right of the midsternal line Heart action was regular and rapid No significant murmurs were heard There was a very distinct tremor of the extended fingers The skin was flushed, warm, and moist Basal metabolism was +73 eleven days after admission and +56 the following day After remaining at rest in bed for forty-five days on the medical service the patient was transferred to the surgical service for operation Partial thyroidectomy was done under local anesthesia by Dr John Homans on November 26, 1915 and about half of the gland and isthmus was removed The patient made an uneventful recovery from the operation On December 31, 1915, January 1, and January 3, 1916 the patient was given treatments with the Roentgen ray On January 8, 1916 the tonsils and adenoids were removed by Dr C B Walker The patient was discharged on January 29, 1916 On discharge his metabolism was +35 and some of his symptoms seemed improved, but there was no marked changes A great deal of interest was expressed at that time concerning the amount of thyroid gland which was removed, and some were of the opinion that it might be necessary to return for a second operation The patient was heard from on February 6, 1916, and stated that he had gained 10 pounds, felt better, and proposed to begin work

His second admission to the hospital was on December 7, 1918, with influenza of a moderately severe nature during the epidemic He gave the history that after resting for a month following his discharge from the hospital, he began to work, doing odd jobs about a machine shop For a year and a half before admission he had been janitor of a theater and he had considered the work fairly hard He had remained well, however, though his pulse had been rapid at times His tremor had disappeared, he had no dyspnea, nervousness, sweating, or loss of weight Physical examination following the patient's recovery from influenza showed slight exophthalmos, a definite lid-lag, a moderate enlargement of the thyroid gland but no

thrill or bruit over the thyroid gland There was a very slight tremor of the extended fingers On December 17, 1918, after the patient's temperature had been normal for seven days, his metabolism was −4, pulse 75 per minute, and body weight 55 7 kg After leaving the hospital the patient continued in good health until April, 1924, four months before his last admission, when following some violent physical work, in the way of lifting, he observed that the right lobe of the thyroid began to swell He became nervous and irritable, was easily excited, and developed palpitation and dyspnea He suffered greatly from the warm weather His appetite had been ravenous, but during the seven months prior to admission he had lost 30 pounds His physical examination at this time was highly characteristic of exophthalmic goiter, as it had been on his first admission to the hospital His metabolism on the day following admission (August 9, 1924) was +55 With rest and Lugol's solution, 5 gtt t i d , it dropped in seven days to +17 The patient was transferred to the surgical service on August 30, 1924, and a second operation was done by Dr F C Newton on September 2, 1924, under gas-oxygen and novocain anesthesia He was discharged September 15, 1924 in good condition

The important points which are emphasized by the history of this patient are these

1 The patient had a recurrence of exophthalmic goiter which manifested itself after eight years of normal health

2 The beneficial effect of iodin as a preoperative measure is well shown during the patient's last admission

The first statement needs little comment Many have the feeling that surgery has accomplished a cure if the patient's metabolism falls to normal limits, there is a substantial gain in weight, and the symptoms disappear for the short interval that the patient remains under observation during the postoperative period Almost all patients show at least a transient improvement or a temporary cure following thyroidectomy, but the most essential information, that is, the duration or permanence of this improvement, is often not available It is of the utmost importance in a disease such as this, with a tendency to recur-

rences, to follow each patient carefully after a subtotal thyroidectomy, as well as those who have had other forms of treatment, until the symptoms have remained absent for a long period of time and the basal metabolism has been persistently within normal limits Judging from this patient's history, one cannot assure a patient who has been free of symptoms for as long as eight years that the disease will not recur, although the possibility of this is not great In 1915, when partial thyroidectomy was first performed on this patient, it was customary to remove a smaller amount of thyroid gland than is removed by most of the present-day surgeons With removal of the greater portion of the gland the results of surgery have been better, although even now apparently the criticism that not enough thyroid tissue has been removed is frequently justified Certainly, it is rare that too much thyroid gland is removed, as postoperative myxedema is at present very infrequently observed The beneficial effect of iodin in a reduction of the basal metabolism is also well shown in this patient, as indicated by a drop to +17 per cent after this drug had been administered for one week Our experience concerning the value of iodin in this condition coincides essentially with that of Means and Starr[6] at the Massachusetts General Hospital, who report an "iodin remission" in about 80 per cent of their patients It has been very rare in our experience that the metabolism has not fallen to the vicinity of +20 per cent or lower after a week or ten days of treatment with Lugol's solution in exophthalmic goiter Following the report of Plummer[7] in 1923, that the administration of iodin was followed by a striking improvement in these patients, its use has been wide-spread More recently, Plummer and Boothby[8] have emphasized the usefulness of iodin in this condition This drug in doses of 5 gtt t i d , is a distinct addition to our treatment of exophthalmic goiter, but it serves its most useful purpose in preparation of the patient for operation as it renders the procedure safer, in many instances, if not all, preliminary thyroid artery ligations may be eliminated, and in addition the patient's convalescence is shortened A further great use of iodin in this disease is in the so-called "thyroid

crisis" associated with gastro-intestinal symptoms and extreme prostration Relief follows almost immediately the use of this drug in combination with other appropriate measures

While the reports concerning the use of iodin in these patients have quite properly been enthusiastic, the harmful effects of this drug have not been emphasized There is, no doubt, a great deal more to be learned concerning the action of iodin in exophthalmic goiter before its real value can be appreciated With our present experience, a few of its dangers may be mentioned It has not, for example, been demonstrated that iodin causes anything more than a purely transient improvement in the patient, and it should not, at least with our present understanding of it, be used in the belief that a permanent cure can be accomplished Apparently the amelioration of symptoms and the decline in the basal metabolism persists for only a brief interval despite the continued use of the drug, even in excessive doses If the patient is operated upon during an iodin remission, it is of utmost importance to continue the dosage, per rectum if necessary, on the day of the operation and until the patient is convalescent If this is not done, there is likely to be a very abrupt release of the iodin effect within a short time, characterized by a rise in the basal metabolism to an exceedingly high level, which may result in the patient's condition becoming precarious Such an effect is particularly true if iodin is discontinued on the day of the operation, or during the immediate postoperative period An additional point concerning iodin therapy in hyperthyroidism is the indiscriminate use of the drug in patients before the diagnosis is firmly established by means of the basal metabolism Patients with atypical hyperthyroidism, in whom the conspicuous signs of the disease are lacking, often present a problem for diagnosis which is most readily solved by careful metabolism studies If iodin is administered to such patients, before the metabolism has been determined, it robs the diagnostician of one of his most valuable aids, for if the metabolism has been elevated it may have been brought to within normal by the therapy The situation under these circumstances is somewhat analogous to the mak-

ing of the symptoms of acute appendicitis by large doses of morphin

The régime which we have found useful at the Peter Bent Brigham Hospital in managing patients with exophthalmic goiter is as follows (1) Lugol's solution (Liquor iodi compositus, U S P) is not given until the diagnosis has been firmly established, and at least two satisfactory metabolism determinations have been obtained (2) The drug is then given in the dose of 5 drops, three times a day, following meals, and well diluted with water During this interval the patient is kept at complete rest in bed, and metabolism determinations are made at frequent intervals, varying from one a day to one every third or fourth day (3) The lowest level of the metabolism curve is usually reached in from one to two weeks and if no complications exist, this low level is considered the optimum time for operation If the patient is not carefully observed and the basal metabolism determined at frequent intervals, it is very easy to miss the point at which the metabolism is lowest The best situation for operative interference is thereby lost, as the metabolism may then slowly rise to a point approximating its initial level (4) The iodin is given on the day of the operation and for a period of from four to six weeks following it It may be unnecessary to continue to use iodin for such a length of time following the operation, as the period selected is a purely arbitrary one which may with further experience be shortened

SUMMARY

The most important facts concerning exophthalmic goiter which are emphasized by the case histories of these 4 patients may be summarized as follows

1 A patient may recover from the disease without any treatment other than avoiding heavy work This recovery may be permanent, in the patient whose history has been reported it has persisted for five years

2 Although temporary recovery may occur in untreated patients, there is a marked tendency for the disease to recur.

Each recurrence is likely to result in additional cardiac injury which may lead to the patient's death

3 Roentgen-ray treatment produces results in a small group of these patients which equal surgery In many, however, it apparently has no effect

4 Following partial thyroidectomy, all of the symptoms may reappear, after eight years of perfect health

5 The administration of iodin to these patients is a valuable preoperative measure, as it is followed by a transient drop in the basal metabolism

The ideal treatment of exophthalmic goiter, that is, the removal of the primary cause has not been discovered, as we are still in the dark concerning the real changes which are responsible for the over- or altered function of the thyroid gland Surgery appears to offer the best opportunity of cure by means of subtotal thyroidectomy, although even in the most expert hands a second resection of the gland and occasionally a third is necessary for the relief of symptoms The operative mortality of the surgeon, who has perfected his technic of thyroid surgery to a high degree, is exceedingly low and this factor, therefore, cannot be used as a valid argument for advising the patient to follow some other form of treatment The tendency for an unknown percentage of patients with this disease to recover without treatment does not argue that treatment should be withheld, for, while a remission may intervene, it is characteristic for a series of waves of the disease to appear which may be responsible for the patient's death in a thyroid crisis, or the production of chronic cardiac disease leading to a life of invalidism The Roentgen ray, while it has a low percentage of apparent cures, is useful if the patient cannot be persuaded to undergo surgery, although it should be discarded after a short trial if the improvement is not striking, as experience has taught us that additional treatment under these circumstances will be of little value Iodin, in the form of Lugol's solution, is of great assistance, as in doses of 5 gtt t i d , it usually causes a prompt drop in the basal metabolism, which persists for only a relatively brief interval It is during this re-

mission that surgery can be performed with the greatest margin of safety

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CLINIC OF DR FREDERICK T LORD

BOSTON

DISCUSSION OF THE DIAGNOSIS IN A CASE OF PRIMARY PULMONARY ACTINOMYCOSIS[1]

THE following case history affords the opportunity to discuss certain aspects of lung-hilus disease and put on record a rare type of primary pulmonary disturbance It is offered with the hope that others will be induced to present the radiographic appearances of similar cases and thus facilitate the earlier recognition of the disease

A G (No 257,851), male, aged thirty-four, was under observation at the Massachusetts General Hospital August 14 to 21, 1923 He had been in good health until six weeks previous to the time the accompanying a-ray film (Fig 231) was taken During this interval there was cough with scanty colorless and odorless sputum, at times streaked with blood Two weeks prior to the time this film was taken he coughed up about 3 teaspoonfuls of blood He was troubled for about six weeks by constant dull pain in the left lower thoracic region, profuse night-sweats, loss of strength and insomnia, and had lost about 12 pounds in weight He had been short of breath for two weeks Physical examination showed an area of dulness in the left back in the region of the lung root and diminished breathing, with numerous non-consonating moist râles at the left base behind There were sibilant râles throughout the left chest back and front The heart was not displaced Other physical signs of pulmonary disease were absent There was no evidence suggesting syphilis in the history or physical examination

The patient had a white count varying from 9500 to 20,000,

[1] In the presentation of this case I have used a photograph and certain data from the new edition of my book, "Diseases of the Bronchi, Lungs, and Pleura," now in preparation by Messrs Lea & Febiger

of which 77 per cent were polynuclear cells, 19 per cent were lymphocytes, and 3 per cent were eosinophils His temperature during a week of observation ranged from 99° to 101° F,

Fig 231 —Primary actinomycosis of lung (No 257,851) Marked increased density at both lung roots, especially the left, where density is soft, with radial projections into lung field Diminished radiance of entire left lung field in consequence of increased linear markings and probably also partial atelectasis Slight elevation of the left diaphragm

with a pulse-rate of about 80 and respiration of 25 The sputum, Wassermann test, and urine were negative Blood-pressure 125/70

The *x*-ray film shows slight narrowing of the left interspaces and elevation of the left half of the diaphragm, the left being normally lower in comparison with the right than is seen here

The most striking feature of the *x*-ray, however, is an increased density at both lung roots, especially the left, where there is an area occupying the region between the aortic knob and the left border of the cardiac shadow Extending from this root shadow are radial projections toward the upper and median parts of the lung field, and these reach the periphery in the lateral aspects of the chest

Discussion —The *x*-ray findings are of assistance in interpreting the physical signs There is some degree of atelectasis of the left lung, although not enough to speak of the condition as massive collapse The diminished breathing and râles at the left base behind are to be ascribed to partial collapse of the lower part of the lung in consequence of the lesion at the left lung root The sibilant râles on the left side may be explained on the ground of some constriction of the bronchi as they pass through the involved region

Varying degrees of collapse of the lung in connection with pulmonary pathology are common, and serve to explain physical and *x*-ray findings otherwise difficult of interpretation The collapse in this case is minor in degree and insufficient to displace the heart toward the affected side, but enough to elevate the left half of the diaphragm, narrow the intercostal spaces, and increase the density of the left lung Minor degrees of pulmonary collapse are a matter of almost daily observation, and modify the physical findings at the bases of the lungs in patients long abed, at the neighborhood of pleural tumors, with pneumothorax, pleural and pericardial effusion, and when the diaphragm is elevated in consequence of tympanites, ascites, or subdiaphragmatic abscess Minor collapse is not infrequent in pneumonia developing at the root of the lung, usually affecting the posterior inferior aspect of the corresponding lung In the absence of cardiac dislocation atelectasis complicating pneumonia is likely to be confused with pulmonary infiltration or a complicating pleural effusion In my records, of 558 cases

of pneumonia personally examined, are 14, or 2 5 per cent , in which the heart was displaced toward the side of the pneumonia Absence of the signs of pleural fluid or air on the opposite side indicates that the cardiac displacement in these cases is to be attributed to massive collapse Pleural fluid may be present on the affected side and the heart be displaced toward that side, as in 2 of the 14 cases Massive collapse in pneumonia appears from my cases to be more common in young persons Although the ages ranged from fourteen to seventy-five, 7 of the 14 cases were from fourteen to seventeen years of age, 9 of the cases were lobar, and 5, bronchopneumonia.

Atelectasis of the lung is common in connection with pulmonary abscess developing at the corresponding root, and the mistake is often made of regarding dulness at the base, with diminished voice, whisper and tactile fremitus, and moist râles as the essential lesion, and to miss an area of dulness higher in the back until the a-ray discloses an area of increased density due to abscess in this region Collapse of the lung causes important physical signs in connection with foreign bodies which completely occlude the bronchi and with malignant disease I have recently observed massive collapse as a complication of hemoptysis in pulmonary tuberculosis

Although the mechanism of massive collapse is not fully understood, all our pneumonia cases have had purulent expectoration, and in these and the remainder of the series there has been reason to suspect bronchostenosis from inflammatory swelling of the mucous membrane, the accumulation of bronchial exudate, new growth, foreign body, or blood-clot as the cause of the disturbance

As regards physical signs there are two groups of cases In the cases of retraction atelectasis, the bronchi remaining patent, there is dulness, bronchial breathing, egophony, increase of voice, whisper, and tactile fremitus In the cases in which the bronchi are plugged there is dulness, diminished vesicular breathing, diminished voice, whisper, and tactile fremitus The diagnosis is difficult or impossible without cardiac displacement toward the affected side and the absence of fluid or air

on the opposite side x-Ray examination is desirable in all cases

Differential Diagnosis —The clinical and radiographic aspects of the case suggest the presence of a malignant tumor developing at the left root and to a less extent also at the right root The cough and the character of the expectoration, pain early in the course of the disease shortness of breath, and loss of strength and weight are consistent with malignant disease Night-sweats are uncommon in malignant disease Fever is usually present The leukocytosis is at variance with uncomplicated malignant disease Neoplasms which develop at the lung root are, however, prone to cause bronchial obstruction, and give rise to leukocytosis in consequence of bronchopulmonary infection in the parts supplied by the occluded passages The absence of purulent expectoration in this case is against secondary inflammatory changes as a cause of the leukocytosis The x-ray appearances are not typical of malignant disease, the shadow being less dense and less sharply outlined than is to be expected in such a condition

The question may be raised as to the desirability of bronchoscopic examination in such a case

A definite diagnosis of malignant disease of the bronchi or the lung root may be made by bronchoscopy, provided a small piece of tissue can be removed for microscopic examination In suspected malignant disease in which the radiographic appearances suggest the possibility of surgical interference it is desirable that every effort be made to establish the diagnosis Not only bronchoscopy, but even exploratory thoracotomy are worthy of consideration under such circumstances

Bronchoscopy has the merit of being a relatively simple procedure Advances in surgical technic especially the use of differential pressure anesthesia, make surgical exploration possible, but at present with some risk Once the diagnosis of bronchial or pulmonary malignant disease is established and found to be confined within such limits as to make removal feasible, partial or even complete lobectomy should be considered in spite of the risks In two instances Sauerbruch has success-

fully removed a malignant tumor from the lung In this case, however, the extent of the process, if malignant, excludes all chance of surgical relief

The question may also be raised regarding the therapeutic use of *x*-ray in such a case If this lesion is malignant it is, with probability, to be regarded as cylindric-celled carcinoma taking its origin from the bronchial mucous membrane or the bronchial mucous glands Deep *x*-ray therapy in this type of new growth has not been successful in our experience There has been no notable amelioration of symptoms or apparent shortening of the course of the disease

There appears, then, to be no justification from the point of view of treatment in this case to pursue the investigation for the purpose of establishing the diagnosis of malignant disease by the application of any diagnostic method, such as bronchoscopy, which may add to the discomfort of the patient, or such as exploratory thoracotomy, which may introduce the possibility of a fatal termination in consequence of the application of the method

Actinomycosis is to be considered In the absence of the finding in the sputum of the organisms characteristic of this disease the decision must rest on the clinical and *x*-ray picture The evolution and grouping of the symptoms is consistent with primary pulmonary actinomycosis, in which, in contrast to pulmonary tuberculosis, pleural pain is a feature in a large proportion of the cases and gradually increasing dyspnea is common Hemoptysis during the course of the disease is not infrequent Perforation of the chest wall is more common in actinomycosis than in any other types of pulmonary disease and occurs in about 80 per cent of the cases Its absence here cannot be raised as an argument against this diagnosis on account of the short duration of the disturbance Fever is almost constant in pulmonary actinomycosis The leukocytosis suggests the presence of an inflammatory process, and the absence of purulent expectoration lends support to the supposition that the leukocytosis is to be referred to the development of the root lesion itself rather than to secondary invasion of the bronchi and lung

in consequence of bronchial obstruction Let us consider the x-ray picture in relation to actinomycosis Actinomycosis is a chronic infection, the lesions of which are characterized by the abundant development of connective tissue The root lesion shown by x-ray with its radial projections into the lung field may represent the development of granulation tissue in the hilus and extension toward the periphery The frequency with which extension to the chest wall takes place in this disease may depend on this tendency of the disease to spread outward Abscess formation in multiple areas is also a characteristic pathologic feature of actinomycosis, each abscess being surrounded by dense connective tissue There is no evidence of abscess formation in the clinical or x-ray picture, but it may be that sufficient time has not yet elapsed for the development of losses of pulmonary substance

The inhalation of a foreign body may also be considered Although there is nothing in the history of this case to suggest such an occurrence, it must be admitted that the usual initial symptoms may be absent and pulmonary changes secondary to the lodgment of the foreign body in the air-passages may be the only evidence of its presence The secondary changes are, however, of a suppurative nature, and purulent rather than scanty colorless expectoration may be expected in a case of foreign body inhalation with a history of six weeks' duration and with such extensive lesions as are indicated in the x-ray film There is no suggestion in the radiogram of a foreign body, but a foreign body non-opaque to the x-ray or so placed as to be obscured by overlying shadows may still be present In addition, the x-ray appearance of the lesion does not suggest foreign body, which, if single, tends to obstruct one air channel and confine the later inflammatory changes to the pulmonary territory supplied by the occluded passage In this case the lesion seems to take its origin from the root and be spreading thence into the upper and lateral aspects of the left lung Foreign bodies tend rather to obstruct the lower than the upper bronchi and the right more often than the left The elevation of the left diaphragm, narrowing of the left intercostal spaces, increased density of

the left lung, suggest partial bronchial occlusion at the left lung root, with consequent atelectasis, but there is nothing sufficiently suggestive of foreign body inhalation to warrant bronchoscopic examination

Tuberculosis is also to be considered There is, however, considerable evidence against it Let us take up the five cardinal indications of probable pulmonary tuberculosis in relation to this problem The evolution and grouping of the symptoms is at variance with the usual complex in tuberculosis, in which pain is rarely a prominent feature The hemoptysis is here not out of a clear sky, but occurs in the course of the pulmonary disturbance The thoracic pain may be ascribed to pleurisy, but the presence of other symptoms make it desirable to classify the pleurisy as secondary rather than primary It is only primary pleurisy which almost invariably indicates tuberculosis From the statement that "other physical signs of pulmonary disease were absent," the inference may be made that there were no moist râles with or without expiratory cough at the apical or subapical region The *x*-ray picture departs very far from the usual appearances in tuberculosis in which there is a fine or coarse mottled increase of density above the anterior portion of the third rib, toward the outer rather than the inner aspect of the lung and extending into the periphery The density here is of an even character and involves the root region with lineal shadows radiating into the periphery I have never seen pulmonary tuberculosis with the clinical and radiographic aspects which this case presents, and tuberculosis can, I think, be excluded with reasonable certainty

Syphilis of the lung may also be considered The region of the root is assumed to be the site of election for acquired pulmonary syphilis Is it possible that this patient has a gumma at the left root, and that the radial projections thence into the lung field are due to proliferated connective tissue of syphilitic origin about the blood-vessels or bronchi? The negative Wassermann test makes this unlikely The history and physical examination are not suggestive of syphilis The adequate clinical establishment of pulmonary syphilis is almost impossible,

although its occasional occurrence can hardly be doubted But even when all such conditions as a history of syphilitic infection, the coexistence with pulmonary lesions of other tertiary manifestations, the absence of evidence of tuberculosis, even negative tests with tuberculin, and repeatedly negative search for tubercle bacilli in the sputum, positive Wassermann tests and improvement under antisyphilitic treatment are fulfilled, there still remain other than syphilitic and tuberculous pulmonary processes capable of giving rise to root lesions which may closely simulate syphilis Adequate establishment of acquired tracheobronchial syphilis and the syphilitic nature of the white pneumonia of Virchow in the inherited disease has been accomplished, but I have thus far not ventured to make a positive diagnosis of acquired pulmonary syphilis

Conclusions Regarding the Diagnosis —The clinical features are in accord with either malignant disease or actinomycosis The absence of purulent sputum and the presence of leukocytosis suggest the possibility that the elevated white count is to be ascribed to an inflammatory process capable of causing leukocytosis, but this alone is hardly sufficient evidence on which to argue for actinomycosis and against malignant disease The *x*-ray picture suggests malignant disease, but differs from malignant disease in the absence of sharp limitation of the increased density at the lung root, and the number and tenuity of the radial projections therefrom into the periphery Up to this time I had never seen the *x*-ray picture of a case of primary pulmonary actinomycosis at this early stage in its development, and made a diagnosis of probable malignant disease

Subsequent Course —About four months later the patient entered the Boston City Hospital The sputum, which was at first scanty and colorless, gradually became more abundant and purulent, and for the last three months amounted to about one sputum box of foul-smelling yellowish material a day About four months before his admission he noted a tender, red, hot swelling in the region of the left scapula persisting to the time of his admission He had been increasingly short of breath and continued to complain of pain in the chest At the time of his

admission he noted a lump on the right upper arm similar to the swelling in the left back Deep beneath the mesial surface of the right femur was a small firm nodule about 2 cm in diameter Actinomycosis granules were found in the sputum, the abscess in the back, the lesion in the right upper arm, and the right leg He died about six months from the onset of symptoms, and at autopsy actinomycosis of the lung, chest wall, vertebræ, skin, and subcutaneous tissue of the leg was found

Remarks on the Case —Actinomycosis is a rare disease It is recorded in the records of the Massachusetts General Hospital in 65 (0 0531 per cent) among 122,408 medical and surgical admissions, or only once in each 1883 cases The disease probably arises as an autogenous infection from organisms harbored in the buccal cavity, with secondary invasion of the cervicofacial tissues by direct extension, and the abdomen and lungs through swallowed or inhaled organisms

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CLINICAL SURVEY OF 1000 CASES ON WHOM BASAL METABOLISM STUDIES HAVE BEEN MADE

THE material for this report is drawn almost entirely from the Out-patient Metabolism Clinic of the Boston City Hospital This clinic has been in operation for nearly five years and has supervision over such general metabolic disorders as nephritis, hypertension, obesity, diabetes, and the various endocrine diseases The basal metabolism studies reported in this paper include tests on selected cases from the Metabolism Clinic and also tests on a large number of unselected cases from the general Out-patient Clinics and the House Services The reason for this is that any visiting physician on a House or Out-patient Service has the privilege of referring patients to the clinic for the sole purpose of a metabolism test Such a practice not only increases the number of tests made but also influences results In other words, this study includes not only cases in which a metabolism test can be considered a routine procedure, but a large group of unselected or doubtful cases in which for some reason the question of a change in the metabolic rate was raised These facts are not without significance because they tend to make a study of this sort much more general and, consequently, much more interesting to the practitioner

The apparatus in use in the clinic is a modification of the original Benedict closed circuit portable respiration machine as manufactured by W E Collins, of Boston For the past two years we have used a Roth flutter-valve attachment in place of a

motor In calculating results the Benedict and Harris standard multiple prediction tables for normal basal heat production have been used It may be of interest to state here that during the course of time represented by this study several portable machines of various makes have been tried out After a comparative study we have come to the conclusion that the machine *mentioned above gives uniformly good results*

It is essential that the study of the basal metabolic rate of any individual should be rated as a piece of work requiring correct technical training on the part of the person doing the test, and experience that enables one to properly interpret each test We must always bear in mind that the mere obtaining of a metabolic rate is not enough The rate obtained must be the "basal" rate of metabolism, for any rate above this may lead to erroneous conclusions In order to obtain a rate that is "basal" there are certain conditions which must be fulfilled before the test is undertaken and during the test itself, but it is not within the scope of this survey to enumerate these conditions insomuch as they are emphasized in any current text on basal metabolism

Assuming that the result of a given test represents a true basal reading, the proper interpretation of such a figure is of great importance The commonly accepted standard is that readings within the range of plus or minus 10 per cent may be considered normal We feel that this is not strictly true For example, we have seen cases in which a result higher than plus 10 per cent did not indicate an increased metabolism, and, on the other hand, there are cases in which a reading which does not go as low as minus 10 per cent indicates a mild hypothyroidism The important point is that in the interpretation of basal metabolic readings the patient's clinical signs and symptoms must be carefully considered As examples of the care that must be taken in the interpretation of results the following two groups of cases are presented

Group A

Case No	Date.	Basal metabolism (per cent from normal)	Body weight (nude—Kg.)	Pulse-rate (basal)	Diagnosis.
I	2/24/22	− 8 7	79 8	52	Obesity Mild
	9/24/24	−13 8	77 4	50	Hypothyroidism
II	8/27/20	+ 4 0	57 9	70	Hypothyroidism
	9/14/20	+ 6 0	58 7	68	
	1/ 4/21	+ 4 0	57 3	62	
	12/11/23	− 5 0	67 2	72	
	12/17/23	− 4 0	66 2	74	
	6/ 6/24	− 6 6	64 1	56	
	7/18/24	−19 7	62 7	62–56	
	9/ 5/24	− 7 1	60 8	56	
	9/26/24	− 4 8	61 6	58	

Case I showed in February, 1922 a basal metabolic rate within normal limits She was suspected of having a mild degree of hypothyroidism, and with the basal metabolism of minus $8\frac{7}{10}$ per cent to substantiate the clinical picture, we made a positive diagnosis of hypothyroidism The patient took thyroid for a few months When she came to us in 1924 she stated that no thyroid had been taken for over half a year At this time her basal metabolic rate was definitely lowered and the clinical picture of hypothyroidism was even more pronounced Thyroid therapy instituted and carried out faithfully at this time resulted in definite improvement in the patient's condition

Case II is especially interesting This woman is a nurse, who showed some clinical evidence suggesting hypothyroidism She first came under our observation in 1920 The first three tests done were all within normal limits, and consequently, we felt that thyroid therapy was not indicated It was not until December 1923, that a suggestion of a lowering of the body heat production could be gained by the metabolism test In July 1924 a basal metabolic rate of minus $19\frac{7}{10}$ per cent was found, and the test at this time was consistent with the diagnosis of hypothyroidism This case points out the value of repeated tests, and also that one must not be led astray regarding a clinical picture even though the laboratory test does not show what is expected

Group B

Case No	Date	Basal metabolism (per cent from normal)	Body weight (nude—kg)	Pulse-rate (basal)	Diagnosis
III	4/11/21	+25 0	45 2	78	Adolescent goiter
	4/28/21	+ 5 3	45 2	88	
	6/10/21	+ 1 1	44 4	80	
	7/ 3/22	+ 9 3	46 0	98–84	
IV	10/ 3/22	+60 5	64 9	118–104	Hyperthyroidism
	10/16/22	+40 7	64 9	90	
	10/31/22	+47 9	61 6	92–82	
	11/ 2/22	+41 9	60 4	90	
V	11/28/24	+20 6	47 9	72	Psychoneurosis
	12/ 5/24	+10 3	48 7	66	

Case III is a girl of nineteen, who was sent to our clinic with a diagnosis of exophthalmic goiter based on fulness in the thyroid region, nervousness, inability to gain weight, and a suggestion of exophthalmus We did not feel that the patient showed clinical evidence indicating an increased body heat production. The result of the first metabolism test (plus 25 per cent) contradicted this conclusion on our part, and because of this a second test was done, which gave a normal result Tests done in June, 1921 and July, 1922 were also normal, and a diagnosis of adolescent goiter was made Treatment for exophthalmic goiter in this case might have caused real harm

Case IV This woman was admitted to the hospital with a diagnosis of a question of hyperthyroidism She had a thyroid gland that was not enlarged to palpation (*i e*, no goiter) It will be noted that after her first metabolism test, which was probably not "basal," the basal metabolic rate maintained a constant level definitely above normal In spite of this (the tests being discredited) she was discharged with a diagnosis of psychoneurosis About a year later she was seen again, and a diagnosis of hyperthyroidism was made After a thyroidectomy this patient's symptoms disappeared and her basal metabolic rate became normal (The tests were done at another clinic) This case emphasizes the fact that if the metabolism tests are

correctly done and the basal metabolic rate maintains a constant level definitely above the normal, we must conclude that pathology somewhere in the body is causing an increased body heat production, and if the clinical picture is consistent with hyperthyroidism the results of the test should serve to clinch the diagnosis

Case V This young man came from the Neurological Outpatient Department, with a diagnosis of psychoneurosis and a question of hyperthyroidism His first metabolism test was consistent with hyperthyroidism, but because there was no true clinical picture of this disease the test was repeated, and gave a normal result, which ruled out hyperthyroidism In this case the first test was not "basal" This type of result in basal metabolic studies stresses the necessity of alway considering the clinical picture when interpreting the result of a metabolism test

Cases IV and V illustrate the value of studying the basal metabolic rate in borderline cases where the differential diagnosis is not clear

Under the discussion of interpretation of results, attention has been drawn to the difficulty of setting a definite normal standard for metabolic rates Each case must be considered as an individual problem In many instances metabolism tests must be repeated several times, before the basal rate can be determined Obviously, therefore, in such a large group as the one under consideration it is impracticable to attempt to classify cases according to their metabolic rates Furthermore, in an unselected group of this sort it is not surprising to find a large number of pathologic conditions represented by only one or two cases It has not seemed advisable to include these in the general discussion Consequently, we are presenting our material under certain broad but not necessarily complete diagnostic headings, simply because the majority of the cases studied are included in such a classification

I Thyroid disease
  1 Simple or benign goiter
    (*a*) Adolescent goiter
    (*b*) Adenoma—colloid or cystic goiter
  2 Toxic goiter
    (*a*) Primary hyperthyroidism
    (*b*) Adenoma with secondary hyperthyroidism
  3 Hypothyroidism
II Cases simulating hyperthyroidism
  1 Neurocirculatory asthenia
  2 Nervousness, rapid pulse, neurasthenia, fulness front of neck
  3 Pulmonary tuberculosis
III Obesity
IV Cardiovascular disease
  1 Hypertension
  2 Nephritis
  3 Cardiac disease
V Endocrine disorders—apart from thyroid disease
  1 Ovarian dysfunction
  2 Pituitary disease
VI Miscellaneous group

I THYROID DISEASE

1 **Simple or Benign Goiter**—(*a*) *Adolescent Goiter* (31 Cases)—Much work has been done on this particular phase of the goiter problem In fact, the indications are that it rightly belongs among the so-called preventable diseases We have very little to add to the general discussion, and can merely emphasize certain important facts Of the 31 cases in our group, 23 had metabolic rates ordinarily called normal, in that they were above minus 10 per cent, but all were below zero, 5 cases gave figures lower than minus 10 per cent, and 3 cases gave figures for the first metabolism test above plus 10 per cent A repeated test, however, gave a reading of zero or below These facts are interesting because they illustrate certain points, as follows (1) Ordinarily cases of adolescent goiter have a minus

metabolism Consequently, x-ray treatments in this group may cause myxedema (2) In certain cases the first test may give a plus reading above 10 Considering the fact that patients with adolescent goiter often display nervous symptoms, tachycardia, flushing, tremor, and some enlargement of the thyroid, the importance of a repeated metabolism test is clear In fact, we have literally rescued one such case from a thyroidectomy On the other hand, in a period of about a year and a half we have watched a case of so-called adolescent goiter change from this particular type to a case of hyperthyroidism In December 1921, this patient's basal metabolic rate was minus $4\frac{9}{10}$ per cent., in November 1922, it was plus $10\frac{5}{10}$ per cent, and in July, 1923 it was plus 30 per cent Furthermore, the change in clinical signs and symptoms corresponded with the change in the basal metabolic rate Strictly speaking, cases of adolescent goiter show none of the clinical signs of an increased metabolism, and basal metabolism studies are really unnecessary as an aid to diagnosis However, instances like the one mentioned above illustrate the importance of repeating metabolism studies in this group over a period of years

(*b*) *Adenoma—Colloid or Cystic Goiter* (51 Cases) —These types are grouped together, first, because they are often concurrent in the same gland, and second, because they present an essentially similar clinical aspect except on palpation This procedure in the case of adenomata elicits a firm rather hard discrete mass, while where the colloid or cystic condition prevails we find a softer, more boggy gland These cases come to the clinic either because of the presence of a goiter or because the question of hyperthyroidism is raised They are of concern chiefly for three reasons (1) Because the adenomata may at some time become malignant neoplasms (2) because there is ever present the possibility of secondary hyperthyroidism, and (3) because they may become unsightly or attain such size as to cause pressure symptoms in the form of difficult swallowing and breathing In general, the basal metabolic readings in this group were well within normal limits However, in certain cases of colloid and cystic goiter the destruction of thyroid

tissue is so great that the gland is incapable of maintaining its full functional activity, and we find clinical manifestations of hypothyroidism as well as a lowered basal metabolic rate

2 Toxic Goiter —(*a*) *Primary Hyperthyroidism* (106 Cases)— Every case in this group gave a basal metabolic rate that was definitely increased It is important when considering this diagnosis to remember that the symptomatology will bear direct relationship to the severity of the disease, and also that remissions are not uncommon In other words, if there is only a slight increase in the functional activity of the thyroid, the evidences of cerebral stimulation, vasomotor disturbances, etc, will be slight, and some may be absent, while, if the gland's functional activity is greatly increased, we will find unquestionable evidence of increased body heat production Between these two extremes many varied pictures of hyperthyroidism are encountered For example, there are cases in which no goiter and no exophthalmus was present, and, on the other hand, we have seen cases where the condition of exophthalmus was a familial or individual characteristic entirely independent of any thyroid disorder

(*b*) *Adenoma with Secondary Hyperthyroidism* (25 Cases) — Here again all our cases have given a basal metabolic rate definitely above the normal The salient features are as follows (1) There is usually a history of a goiter of many years' duration, so that when these cases—as a rule, benign adenoma in the beginning—become toxic the patients are past their youth and early adult life, (2) the clinical manifestations of this group are in no way different from the primary cases except that in many instances the toxicity is less severe, (3) these cases are treated surgically, as the adenomata should be removed, and also because the thyroid toxicity does not respond to x-ray therapy as well as in some cases of primary hyperthyroidism, (4) an intrathoracic goiter may be present even though there is no visible enlargement of the thyroid The x-ray is of inestimable value in the diagnosis of this condition

3 Hypothyroidism (88 Cases) —It is pertinent here to say a few words about basal metabolic standards, especially

minus rates We have intimated above that strict adherence to the plus or minus 10 standard may lead to erroneous conclusions This is particularly true in the consideration of minus readings because slight changes on the minus side of the scale are much more significant than similar changes on the plus side For example, we have seen many cases presenting clinical signs of a lowered metabolism where the basal metabolic rate was above minus 10 In other words, a careful history and physical examination must be a part of every basal metabolism study if results are to be of any value The practice of depending entirely upon the basal metabolism test will only lead to trouble Our answer to the question, then, What do we consider an abnormally low basal metabolic rate? would be, Given a patient with clinical signs suggesting a lowered metabolism, any metabolic rate definitely below the zero mark might be considered abnormal

In considering a disorder like hypothyroidism it is, of course, natural that patients may differ greatly as to the number and severity of signs and symptoms For the purposes of discussion, therefore, we have subdivided this group into (1) typical hypothyroidism, corresponding to typical myxedema, and (2) mild or doubtful hypothyroidism

1 *Typical Hypothyroidism* (51 Cases) —The clinical picture presented by a case of typical myxedema is too well known to be described again here There were, in all, 51 such cases where metabolic rates varied from minus 18 to minus 48 per cent As a result of our study of this group there are a few observations which seem worthy of mention

(*a*) It is apparent to us that myxedema is either more common than has been thought or else the diagnosis is often overlooked For example, several of our cases had been under treatment at various clinics for a period of years before the correct diagnosis was made The most common incorrect diagnoses in such instances were nephritis, secondary anemia, and Addison's disease

(*b*) Heretofore it has been a common practice to prove the diagnosis of myxedema by means of a therapeutic test Such

a practice may lead to erroneous conclusions In one of our cases it appears from the records that the diagnosis of myxedema was considered some three years ago, but because the patient did not respond to 9 grains of thyroid daily the diagnosis was considered wrong Now, as a matter of fact, this patient required 75 grains of thyroid a day before her metabolic rate returned to normal and before clinical improvement was complete

(*c*) In order to treat hypothyroidism properly repeated metabolism tests at regular intervals are necessary It is often very difficult to judge the proper thyroid dosage without the aid of metabolism tests

2 *Mild or Doubtful Hypothyroidism* (37 Cases) —In addition to the cases of typical hypothyroidism there is a perfectly definite group of patients whose clinical and basal metabolic study places them in the hypothyroid group In general, the clinical characteristics of this group are as follows (1) Obese, (2) more or less general weakness, with occasional so-called weak spells, (3) inability to withstand cold weather, (4) a certain amount of dryness of the skin, (5) some retardation of mental processes

These patients have a minus metabolism which is generally not marked We have studied 37 such cases where metabolic rates varied between minus 5 and minus 20 per cent This group is too small to warrant very definite conclusions, but there are certain points which are worthy of mention

The fact that obesity is a constant condition is of interest, because it suggests that obesity may be associated with a mild endocrine disorder in many more instances than has been taught heretofore As a matter of fact, it is our experience that these patients do not respond to dietary treatment alone, but they do respond very satisfactorily to a low calorie diet plus small doses of thyroid At any rate, a metabolism test should constitute part of the routine study of every case of obesity

A careful study of a few of the patients in this group suggests that hypothyroidism may be a progressive disorder For example, in Case I, Group *A*, mentioned above, it will be noted that the

first metabolism test gave a reading of only minus $8\frac{7}{10}$ per cent, and it was not until two years later that the reading became definitely below normal (minus $13\frac{8}{10}$ per cent) according to generally accepted standards During this time the patient received no thyroid therapy and her clinical symptoms became much more definite Such a case illustrates not only the importance of repeated metabolic studies over a long period of time but also illustrates how the diagnosis of hypothyroidism might easily be missed for several years

II. CASES SIMULATING HYPERTHYROIDISM (105 CASES)

This is a most interesting group of patients insomuch as in every instance the diagnosis of hyperthyroidism was considered and, in many instances, actually made The group is made up of such clinical conditions as neurocirculatory asthenia, neurasthenia, together with cases of "nervousness," cases showing a rapid pulse fulness in front of the neck, and a few cases of pulmonary tuberculosis The group numbers 105 patients, and in not a single instance was the true basal metabolic rate above normal Attention is called to the use of the term "true basal metabolic rate" because it is in cases of the sort mentioned above that initial basal metabolic rates are so often above normal Repeated tests, however, always show the true state of affairs Too much emphasis cannot be given this point because of the erroneous conclusions so often drawn For example, we have known of several instances where an *x*-ray treatment was credited with reducing a basal metabolic rate of, say, plus 20 per cent to normal, where, without any question, the same result could have been recorded by merely repeating the metabolism test Moreover, cases of this particular type do not present the clinical picture of an increased metabolism Such patients may be nervous, they may have a rapid pulse, a coarse tremor, their eyes may suggest exophthalmus, and there may be some loss in weight, but the patient's skin is cold, not warm, there is no increased perspiration, and no real exophthalmus In other words, these are not cases of hyperthyroidism either clinically or as judged by a basal metabolism test

III OBESITY (81 CASES)

The relationship between obesity and a mild form of hypothyroidism has already been discussed Ordinarily most cases of obesity are looked upon as problems in dietetics, in fact, some observers say that over 90 per cent of the obese can be so classified On this point our observations are not in agreement For example, in the total group of 118 cases of obesity, which includes the 37 cases of mild hypothyroidism mentioned above, only 81, or $68\frac{6}{10}$ per cent, gave metabolic rates well within normal limits We appreciate that this is a comparatively small group, and therefore we are not ready to do anything more than merely record the observation Obviously, in the obese cases where the metabolism is normal, thyroid therapy is not indicated In this connection we have seen harmful results in several instances where thyroid had been prescribed empirically

IV CARDIOVASCULAR DISEASE (76 CASES)

Under this heading we have included three clinical conditions (1) Essential hypertension, (2) chronic nephritis, with or without hypertension, (3) cardiac insufficiency Taking the group as a whole, there were 76 cases In general, the metabolism results were not remarkable, with the exception of 2 cases of essential hypertension and 2 cases of auricular fibrillation in whom the results are worthy of mention Both of the cases of essential hypertension were women between the ages of fifty and fifty-five Neither had any clinical signs of a lowered metabolism nor any demonstrable evidence of renal impairment The metabolic rates were as follows minus $14\frac{6}{10}$ per cent and minus 23 per cent Unfortunately, it has been possible to study only one of these cases carefully Her clinical record is given below

Patient, a Jewess, fifty-one years old, who entered the hospital for relief of headaches and dizziness Menstrual periods have not entirely ceased, but have been irregular during the past year Physical examination was not remarkable except for obesity and hypertension, weight $173\frac{1}{2}$ pounds, blood-pressure

210/120 Careful laboratory study revealed no evidence of kidney impairment

Basal metabolism studies The initial basal metabolic rate was minus $14\frac{5}{10}$ per cent Because of this thyroid therapy was started, and at the end of two weeks the metabolic rate had risen to zero During this time the blood-pressure dropped to 150/100, the weight to 170 pounds, and the clinical symptoms entirely disappeared

This case represents a rather typical syndrome, namely, menopause, obesity, hypertension, and suggests the importance of basal metabolic studies because of the possibility of mild thyroid dysfunction

The 2 cases of auricular fibrillation turned out to be cases of hyperthyroidism without demonstrably enlarged thyroid glands The metabolic rates in these 2 cases were plus 37 per cent and plus 70 per cent This condition has been mentioned in the literature during the past few years and suggests the following dictum Given a case of auricular fibrillation with a doubtful or negative previous cardiac history, look for hyperthyroidism

V ENDOCRINE DISORDERS—APART FROM THYROID DISEASE (14 CASES)

We have had 2 cases of ovarian dysfunction and 12 cases of pituitary dysfunction in this series Clinical pictures that might be referable to others of the endocrine chain have not been seen Certain of these cases have shown, in addition to the manifestations of either ovarian or pituitary disorders, stigmata suggesting a coexisting alteration of thyroid function Where there has been no clinical or metabolic evidence of decreased thyroid function, we have not included thyroid extract in our therapy, and, furthermore, it has been our experience that in such cases there has been little or no response to other types of glandular therapy On the other hand, in cases where we have had evidence justifying the administration of thyroid extract along with the other glandular products, we have noted definite improvement This leads us to believe that in endocrine dysfunction particularly of the ovaries and pituitary the

improvement resulting from glandular therapy is to a large degree dependent on the correction of the thyroid disorder There is yet much to be done before the effectiveness of treatment in ovarian and pituitary disorder is equivalent to that seen in thyroid disease

VI MISCELLANEOUS GROUP (423 CASES)

Under this classification we are including a large number of cases representing a considerable variety of pathologic conditions In most instances the number of cases illustrating a given disease is too small to be worthy of any special comment There, are, however, a few groups which deserve attention because the study of the basal metabolism suggests the advisability of a more complete investigation

1 **Chronic Arthritis** (13 Cases) —Eight of the cases of this group, or 61 per cent, gave metabolic readings below normal Moreover, in the cases which did show a definitely minus metabolism, thyroid therapy seemed to help the arthritic condition This suggests that chronic arthritis may be part of a general metabolic disorder, and that treatment which tends to improve the general metabolism may improve the arthritic condition It will be extremely interesting to collect such data from a large group including the various types of joint troubles

2 **Certain Chronic Skin Disorders** (14 Cases) —In this group there are 9 cases of ichthyosis and 5 of acne vulgaris Five of the cases of ichthyosis and two of the cases of acne gave metabolic rates below normal, and in these cases thyroid therapy gave promising results

3 **Vasomotor Rhinitis** (8 Cases) —All of the cases of this group gave basal metabolic rates definitely below normal, and here again thyroid therapy resulted in considerable improvement

It seems advisable here to interpose a word of warning in regard to the interpretation of metabolic results in the three groups mentioned above It is quite possible that thyroid therapy may be a valuable aid in the management of such cases, but the performance of a metabolism test should not be the one

deciding factor There must be clinical evidence to supplement the basal metabolic study This involves careful co-operation between the specialist, the clinician, and the laboratory It is our impression that this sort of co-operation does not always exist, but we feel that it must be insisted upon in order to interpret correctly the basal metabolic studies of any group of cases

The remaining 391 cases in this group represent fifty-four definite pathologic conditions However, the number of cases in any one group is so small that any special comment seems unwarranted It is sufficient to say that in the vast majority of these miscellaneous cases the metabolic rate was normal

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CLINIC OF DR HERRMANN L BLUMGART

BOSTON CITY HOSPITAL

VENOUS PRESSURES THEIR CLINICAL SIGNIFICANCE[1]

STARLING has shown that over a wide range of values an increase in the amount of venous blood delivered to the heart results in a corresponding increase in the minute volume output There is a maximal value, however, beyond which any particular heart is incapable of increased response When the amount of venous return to the heart exceeds this value it is clear that the blood must accumulate in the veins This train of events occurs not only in the veins of the peripheral circulation, but likewise in the vessels of the lesser circulation The former condition is evidenced by a rise of peripheral venous pressure as directly measured, the latter condition is indirectly reflected by a decreased vital capacity of the lungs

Measurement of the venous pressure and determination of the vital capacity derive their great importance from the fact that they indicate that the heart has been called upon for more work than it is capable of performing In other words, under the usual conditions of life an increased venous pressure and a decreased vital capacity indicate the onset of decompensation

The venous pressure has been determined in our patients by the method of Moritz and Tabora and that of Gaertner The method of Moritz and Tabora is admittedly the most direct and the most accurate A hollow beedle is introduced directly into the vein The needle is connected to a fluid column manometer in which the height of the fluid is well above the expected pressure in the vein After withdrawing a small amount of

[1] From the service of Dr Francis W Peabody, Boston City Hospital

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blood in order to be certain that the venipuncture is satisfactory, one turns a three-way stop-cock so that the needle is connected to the manometer The fluid in the manometer column falls until the pressures of the venous blood and the fluid column become equalized The height of the fluid in the manometer system above the level of the heart represents the venous pressure The level used by Moritz and Tabora differs from that used by Gaertner, and since I wish to compare the results obtained by these two methods I have used the zero level advised by Gaertner, namely, the costoxyphoid angle The difference in level between the top of the manometer fluid column and the costoxyphoid angle can easily be determined by the use of a carpenter's level and square

Although the method of Moritz and Tabora offers the most accurate readings, the necessary aseptic precautions and the pain attendant to venipuncture make the procedure somewhat difficult as a clinical routine I have therefore first estimated the venous pressure in each of these patients by the method of Gaertner to learn whether the readings by this method are sufficiently accurate for clinical purposes The procedure is simple, consisting solely in observing a superficial vein of the hand or arm while the arm is slowly raised, and noting the height above the costoxyphoid angle at which collapse occurs It is interesting to note that this latter method gives results which are of considerable clinical value Care must be taken that the arm is comfortable, relaxed, and absolutely free from external compression Moreover, since Hooker has shown that diurnal variations in the venous pressure occur, it is advisable, in order that the readings be more strictly comparable, to make the various determinations at the same time of day No reading by the method of Moritz and Tabora should be considered valid unless the respiratory excursions of the fluid column are readily discernable In a series of normal individuals the venous pressures determined by these methods were in no instance found to be above 5 cm

The significance of venous pressure determinations can perhaps be best illustrated by considering the following 2 patients

The first patient is a married man of thirty-three, who entered the hospital complaining of shortness of breath and swelling of the legs His past history is negative save for rheumatic fever at six with redness, swelling, and tenderness of various joints Ten years previous to his present entry he suffered from breathlessness, cough, and precordial pain, forcing him to remain in bed for two weeks His symptoms gradually diminished during his stay in bed, and he was able to return to his work as a clerk He then felt perfectly well until two weeks ago, when he was troubled by a head cold, and noted the onset of cough and breathlessness on exertion His symptoms gradually became worse, and he was finally forced to go to bed ten days ago Physical examination at that time showed a well-developed and well-nourished man sitting up in bed moderately dyspneic The skin and mucous membranes were deeply cyanotic Examination of the heart showed moderate cardiac enlargement, regular rhythm, with a rate of 90 At the apex a low-pitched rumbling middiastolic murmur led up to a snapping first sound, and was followed by a soft systolic blow The second sound was not accentuated Examination of the lungs showed normal resonance, normal breath and voice sounds, save that from the midscapula to the base many medium moist râles were audible The liver and spleen were not palpable Slight pitting edema was evident over the sacrum and both tibia His blood-pressure was 126/72 His venous pressure by the method of Gaertner was 18 cm , by the method of Moritz and Tabora, 21 4 cm His vital capacity was 1100 c c

On rest in bed and digitalization his breathing became less labored, his edema lessened On the fourth day his vital capacity had increased to 1400 c c and his venous pressure had decreased to 14 5 cm by the method of Gaertner, by the method of Moritz and Tabora, to 16 cm Today his lungs are clear, his vital capacity has risen to 1800 c c , and his venous pressure by the method of Gaertner is 12 cm , by the method of Moritz and Tabora, 10 cm

In a series of normal individuals the venous pressures determined by these methods were in no instance found to be above

5 cm In this patient there are no signs of edema, the lungs are clear, and were it not for this slight but definite increase of venous pressure we would be justified in allowing the patient to get out of bed It should be evident from the previous discussions, however, that the increase of venous pressure signifies that the heart is not capable of transferring all the venous blood offered it to the arterial side Surely if we allow the patient up out of bed his heart will be incapable of coping successfully with a further increase in the amount of work it must perform Allowing him out of bed will inevitably result in a prolongation of his convalescence if it does not result in an actual recrudescence of the signs and symptoms of decompensation If we had not made determinations of the venous pressure in this case we might have erred seriously in the management of his convalescence

The second case to be presented is a married wood-turner of thirty-six, who entered the hospital ten days ago complaining of shortness of breath His past history contained no significant data He felt perfectly well until four and a half years ago, when, while working, he first noticed the onset of gastric distress, precordial pain, breathlessness, and edema of the ankles He remained in bed for two weeks, and then, by carefully restricting his activity, enjoyed apparently good health until eight months ago, when he was forced to enter a hospital because of increased breathlessness He stayed at that hospital for five weeks, was relieved of his symptoms, and returned home Three weeks ago, following a period of overexertion, he again noticed increasing breathlessness, slight swelling of his legs, and substernal tension Two weeks ago he began to be troubled by cough and nocturnal dyspnea, and he had to sleep on four pillows at night to be comfortable These symptoms increased in severity, so that he was finally forced to enter this hospital eleven days ago Physical examination showed conspicuous grayish cyanosis, regular deep respirations, 24 per minute, and normal temperature A moderate number of medium to coarse moist râles were heard at the bases of both lungs posteriorly His heart showed moderate enlargement

The impulse was diffuse, not forcible, and best felt in the sixth interspace The heart action was absolutely irregular, with ventricular rate of 150 and a pulse at the wrist of 120 The liver and spleen were not palpable There were no signs of fluid in the abdomen, no demonstrable edema over the back, sacrum, or legs His venous pressure by the method of Moritz and Tabora was 25 4 cm , by the method of Gaertner, 22 cm His vital capacity was 2400 c c On rest in bed and digitalization during the next four days his general condition improved, as evidenced objectively by a fall in ventricular rate to 74, the disappearance of the pulse deficit, a rise in vital capacity to 2950 c c , and a fall of venous pressure to 19 2 cm by the method of Moritz and Tabora, and to 19 cm by the method of Gaertner

Three days ago his heart rate had dropped to 62, he felt nauseated, and digitalis was discontinued Physical examination of the lungs continued to show many medium to coarse râles His vital capacity was 2450 c c , his venous pressure by the method of Moritz and Tabora, 19 cm , by the method of Gaertner, 18 cm

Today his signs on physical examination remain essentially the same and his venous pressure by the direct method is 19 cm , by the indirect method, 21 cm His vital capacity is 2500 c c

The high venous pressures in this patient indicates that his heart is incapable of maintaining the rate of blood flow necessary for the needs of his body A continued high venous pressure despite rest and digitalization invariably indicates that the prognosis is grave

The patient has complained of nocturnal dyspnea I have observed him at night As he falls off to sleep his breathing becomes Cheyne-Stokes in character In the last part of the period of apnea he awakens with a choking sensation and is troubled by dyspnea The administration of caffein to these patients, by increasing the irritability of the respiratory center, frequently serves to allay these attacks of nocturnal dyspnea

The question of the etiology of orthopnea is an interesting one Some believe that these patients experience greater comfort sleeping in the upright position because of the mechanical

aid this gives to the diaphragm and respiratory muscles I have often wondered whether increased venous pressure might not also be a factor in the causation of orthopnea Starling and Tubby as far back as 1896 showed that capillary stasis was consequent to high venous pressure It seems possible, therefore, that these patients by sitting in the upright position effect a decrease in venous pressure in the veins of the medulla, and particularly in those veins about the respiratory center, resulting in an increased blood-supply to the respiratory center If, for example, a patient with a venous pressure of 10 cm sits up so that his respiratory center is 10 cm above the right auricle, it follows that the pressure in the veins about the respiratory center will be zero In patients with cardiac decompensation suffering from orthopnea I have measured the distance of the occipital protuberance above the second right interspace, and found a rather surprising correlation between this distance and the venous pressure as measured by the method of Moritz and Tabora

CLINIC OF DR WILLIAM P MURPHY

PETER BENT BRIGHAM HOSPITAL

FIVE CASES OF DIABETES AND COMA[1]

Case I The Effect of Three Attacks of Coma Upon Tolerance
Case II. Infection and Coma
Case III An Obscure Case of Coma
Case IV Coma Due to Cerebral Hemorrhage Simulating Diabetic Coma
Case V. Renal Insufficiency Simulating Diabetic Coma

As it is of the greatest importance to recognize coma resulting from the acidosis of diabetes because of the specific value of insulin in treatment I shall present in this clinic 5 cases which illustrate various interesting aspects of severe diabetes

Case I The Effect of Three Attacks of Coma Upon Tolerance —A housewife, forty-one years of age, of English descent, entered the hospital for the first time in May, 1923 Her family and past history showed little of importance Four months before her first admission she had noticed increasing thirst, polyuria, and fatigue In spite of the fact that her appetite was excessive, she had lost 30 pounds in weight during this four-month period Physical examination was negative except that the tonsils were enlarged, all of the teeth were out, and there was a considerable degree of emaciation The urine contained a great deal of sugar at entry, but became sugar free in five days without insulin, and the patient was discharged in good condition on a 2000 calorie diet

Since her first admission this patient has re-entered the

[1] From the Medical Clinic of the Peter Bent Brigham Hospital, Boston, Mass

hospital on three occasions, each time with a severe acidosis and in a comatose or semicomatose state Before the first attack of coma she developed an acute respiratory tract infection which no doubt helped to produce acidosis The two subsequent attacks were caused largely by her failure to follow the prescribed dietary régime At each attack of coma she received treatment in the hospital approximately three hours after the onset of an alarming acidosis

The treatment employed was as follows She was at once wrapped in blankets and warmed with hot water bottles A urine sample was obtained by catheter for an immediate diagnosis, after which fluids were forced by means of rectal drip of plain water, subpectoral injections of normal saline solution, and water by mouth after gastric lavage Following a chemical examination of the blood, to determine the blood-sugar concentration and the degree of acidosis, insulin was given subcutaneously and intravenously about every two hours, starting with an initial dose of between 25 and 40 units Each succeeding dose of insulin was determined by the amount of sugar in the urine or blood at two-hour periods As the patient became conscious she was encouraged to drink orange juice in order to prevent the possibility of hypoglycemia and to afford a liberal supply of easily available sugar On each admission the patient responded rapidly to treatment, and was subsequently discharged with a new food-insulin balance

In the table given on p 1519 is a summary of the main points of interest from a laboratory point of view of the four admissions of this patient

The admission blood-sugar and CO_2 combining power determinations as shown in the table indicate the clinical condition on each admission, as does the diacetic acid reaction in the urine in this case The urinary sugar determinations were done on single specimens, so are of little value except to indicate diabetes The blood-counts are of interest because they all tended to be high on admission and, except in the case of the red cell count on the last admission, dropped after treatment Such a change in the blood-count is common in coma cases, and is probably

TABLE 1

The Progress of Imperfectly Treated Diabetes

Admission condition Period in hospital		No acidosis May 19 to June 6, '24	In coma Mar 25 to May 12, '24	Semicomatose Sept 3 to Sept 27, '24	In coma Nov 25 to Dec 23, '24
Admission blood sugar	Mgm per 100 c c	210	470	160	570
Admission blood CO_2	Volumes per cent	49	20 2	24 1	12 6
Admission urine sugar	Per cent	5 0	4	1 8	4
Admission diacetic acid	Qualitative	+	+ +	+ +	+ + +
Admission hemoglobin	Per cent	120	100	86	80
Admission red blood count	Millions per c mm.	4 7	5 5	5 2	3 9
Admission white blood count	Per c mm	8,800	30,000	14,400	14,600
Insulin on first day	Units	0	110	75	100
Insulin on discharge	Units	0	30	30	30
Total glucose of diet on discharge	Grams	128	111	96	87
Body weight at entry	Kg	46 6	37 2	40 0	40 8

the result of dehydration, and may be relieved by forcing fluids A point of particular interest is the change in food tolerance which has occurred during this period of approximately twenty months The total glucose tolerance apparently has dropped from 128 grams without insulin to 87 grams with 30 units of insulin daily It is difficult to tell whether this loss in tolerance is a result of the recurring acidosis or due simply to failure to keep the urine sugar free through proper dieting In any event this case demonstrates quite strikingly the effect on a patient with diabetes of failure to observe the prescribed dietary régime Severe acidosis resulting in coma was produced on two or possibly three occasions After each attack of coma the patient's glucose tolerance was found to be lower than at each preceding observation There was a weight loss of approximately 6 kilograms during this entire period The diabetes appears to have become steadily and progressively worse as time has gone on This is the penalty which carelessly managed cases are called upon to pay

Case II Infection and Coma—A Jewish housewife, sixty-four years of age, was admitted to the hospital in a comatose condition at 11 50 P M on December 13, 1922, about seven hours after the onset of coma The family history showed that one aunt had diabetes The patient's past history was that of a woman in general good health, stout, and a hearty eater Eight years before this admission to the hospital sugar was found in the urine following an acute illness of three weeks' duration, during which she had vertigo, nausea, vomiting, fever, dry mouth, burning on micturition, and a loss of 10 pounds in weight She then followed a prescribed diabetic diet for six years, losing about 20 pounds in weight during the interval After six years of treatment she "broke over" her diet, with a return of diabetic symptoms, and was again made to diet more carefully, so that she kept in fairly good condition for two years About one week before entering the hospital in December, 1922 she had a "common cold," from which she apparently recovered Two days before admission she felt weak, had a headache with gen-

eralized aching, which lasted until the morning of the day of admission She did her usual morning housework, but toward 5 in the afternoon became drowsy, and thereupon rapidly went into coma Physical examination after admission to the ward showed deep, difficult breathing, flushed face, red, dry tongue, and "acetone" breath There were a few crackling râles over the left lower lobe of the lung, with a suggestion of consolidation The abdomen was distended with gas The blood-sugar concentration was 840 mgm per 100 c c and the CO_2 combining power 11 9 volumes per cent The urine sugar determined on a single catherized specimen was 3 3 per cent, with a single plus diacetic reaction and a specific gravity of 1 018 The hemoglobin was 109 per cent, the red cell count 5,600,000, and the white cell count 40,000 per cmm The temperature on the night of admission was 96 2° F, but rose to 100° F by the following morning Treatment was carried out as described in the first case except that smaller doses of insulin were given In the afternoon of the day following admission the temperature had increased the coma, which had been partially overcome, deepened, and the patient died at 10 30 P M on December 14, 1922 Postmortem examination revealed extensive bronchopneumonia, with edema and congestion of the lungs, cholelithiasis, and acute splenitis

Although the pulmonary infection was undoubtedly the most important factor in producing the acidosis which resulted in coma and death, more careful observance of dietary rules should have kept this patient from developing such a severe degree of acidosis and should have increased the chances of recovery The blood-picture was again suggestive of a highly concentrated blood, although the white cell count was too high to be explained on that basis alone

A comparison of these 2 cases is of interest from the standpoint of prognosis in coma The first case undoubtedly had as severe a diabetic process as did the second case Yet the first case has recovered from coma three times, whereas the second case, with a severe complicating infection, died Our experience leads us to believe that cases of uncomplicated acidosis

and coma usually recover easily and quickly with insulin treatment, while the cases complicated by a severe infection do not recover unless the acidosis be relieved before actual coma has set in Therefore the prevention of coma depends not only upon adherence to diet but also, in part, upon the prevention of severe infections

In order to illustrate the difficulties sometimes encountered in diagnosis the following cases may be of interest

Case III An Obscure Case of Coma —A colored physician and preacher, fifty-two years of age, had symptoms suggesting diabetes for one year before entering the hospital Until five days before admission he had kept at his regular work, although feeling weak He then suddenly became nauseated, vomited, and had marked polydipsia and polyuria It is not known whether or not he had fever

Two days before entry he had severe generalized abdominal cramps, and on the day before admission he became unconscious A physician, who examined him at that time, found a large trace of albumin and numerous casts in the urine, and therefore concluded that the patient had uremia Physical examination at entry to the hospital was essentially negative The ophthalmoscopic examination showed nothing unusual The heart and lungs were negative The blood-pressure was 96 systolic and 48 diastolic The abdomen showed no local tenderness or masses and the reflexes were all present A catheter specimen of urine had a specific gravity of 1 030, a trace of albumin, 5 per cent of sugar, a moderate amount of diacetic acid, and an occasional hyaline cast in the sediment The blood-sugar concentration was 840 mgm and the blood-urea nitrogen concentration was 61 mgm per 100 c c, while the blood CO_2 was 34 2 volumes per cent The hemoglobin was 110 per cent, the red count 5,600,000, and the white count was 9800 Did the patient have diabetic coma? Treatment was carried out as described in the previous cases 25 units of insulin was given and repeated in two hours The patient, however, did not show improvement, but died a few hours later A complete

necropsy was not made, the kidneys showed evidence of only a very moderate degree of chronic nephritis There was no demonstrable infection within the abdominal cavity The heart, lungs, and skull were not examined

The history of this case is compatible with diabetes, and abdominal cramps are not uncommon at the onset of severe acidosis The urinary findings of albumin and casts, associated with a blood-urea nitrogen concentration of 61 mgm per 100 c c of blood, are not uncommon in diabetic acidosis On the other hand, so high an alkali reserve as 34 volumes per cent is unusual in diabetic coma unless the patient has taken large doses of soda, and we have no way of knowing whether or not this patient had received any alkali during his sickness As the postmortem examination showed but little kidney damage, and as no other complicating factors were demonstrated, we may consider this to be a case of diabetic coma We cannot be certain of the diagnosis, however, despite a careful physical examination, chemical studies of the blood, and a pathologic examination of the abdominal viscera

Case IV. Coma Due to Cerebral Hemorrhage Simulating Diabetic Coma—A Jewish housewife, fifty-two years of age, was known to have had diabetes for three years and had been on a diet during most of this time Her urine was tested about once each month by her physician Three weeks before the present illness she had only a trace of sugar in the urine On the morning of the day on which the present illness began she felt well At noon, while telephoning, she became unconscious and fell to the floor, but was later able to talk and to walk to bed Two and a half hours later her physician gave her morphin by mouth Shortly thereafter, although there was no evidence of paralysis, she was unable to talk About five hours later morphin was again given because of restlessness The patient then became unconscious and was finally brought to the hospital, approximately twenty-three hours after the onset. Physical examination showed pinpoint pupils, slight spasticity of left arm, equal and sluggish knee-jerks, a positive Babinski

reflex on the left side, and no ankle-clonus The temperature was 102° F , the pulse-rate 120, the respiration rate 35, and the blood-pressure 200 systolic and 105 diastolic A catheter specimen of urine had a specific gravity of 1 025, contained a trace of albumin, 2 8 per cent of sugar, a triple plus diacetic acid reaction, and the sediment contained numerous hyaline and fine granular casts The blood-sugar was 322 mgm per 100 c c of blood and the urea nitrogen was 22 mgm per 100 c c of blood The CO_2 was 51 volumes per cent The hemoglobin was 120 per cent , the red count 5,936,000, and the white count 19,400 Fifteen units of insulin was given at 1 00 P M , and repeated four hours later During the afternoon, two hours after the second dose of insulin, the pulse gradually increased to 140 and the respiration dropped to 15 This change and the appearance of the patient suggested a possible hypoglycemic reaction, so glucose was given by rectum as a safeguard while the sugar content of the blood was determined This was not low The condition did not improve and the patient died about twelve hours after entry The clinical diagnosis of cerebral hemorrhage and diabetes mellitus was made A postmortem examination, not including the brain, showed arteriosclerosis, coronary sclerosis, and chronic vascular nephritis

Several difficulties in diagnosis were encountered in this case The large amount of diacetic acid in the urine was suggestive of acidosis, yet the CO_2 combining power did not indicate a sufficient degree of acidosis to produce coma The blood-pressure was elevated, which is unusual in coma There was evidently a certain amount of nephritis Another diagnostic difficulty arose after insulin had been given, when symptoms occurred which suggested a hypoglycemic reaction While the indications for treatment in this case were not entirely clear cut and definite, certain generalizations from it are justifiable Cerebral hemorrhage in a diabetic patient may produce a clinical picture not unlike diabetic coma All diabetic cases in which acidosis is found should be treated at the earliest possible moment with insulin Insulin does not interfere with the subse-

quent treatment of any complicating condition and may prove to be a life-saving measure On the other hand, insulin should not be given to cases in coma unless diabetes is known to exist In atypical cases insulin should not be given unless the blood-sugar concentration is much elevated and unless the alkali reserve is depleted Diabetic coma does not occur when the blood-sugar concentration and the alkali reserve are normal, even though the bladder urine may contain sugar and diacetic acid

Case V Renal Insufficiency Simulating Diabetic Coma — A paymaster, sixty-six years of age, was known to have had diabetes for six years previous to his entry to the hospital During this time he had polyuria, polydipsia, and nocturia once or twice a night For four years before admission the nocturia had increased somewhat, and he had developed increasing difficulty in passing his urine, often taking ten minutes to start the stream For two weeks before admission to the hospital he had become very drowsy, and for a few days had been delirious or in stupor Physical examination was essentially negative on admission except for a slightly uriniferous odor of breath, a moderately enlarged and hard prostate with a distended bladder, and a temperature of 100 2° F A catheter specimen of urine showed 2 5 per cent of sugar, no diacetic acid, no albumin, and rare hyaline and fine granular casts in the sediment The blood-sugar concentration was 650 mgm and the urea nitrogen concentration was 41 mgm per 100 c c of blood The blood CO_2 was 65 1 volumes per cent The hemoglobin was 100 per cent, the red count 5,060,000, and the white count was 9760 Because of the lack of acidosis despite the high blood and urine sugar concentration the patient's stupor did not appear to be due to diabetic acidosis, it seemed that the coma was uremic in origin due to back-pressure from prostatic obstruction, and that the diabetes was merely a complicating factor With this idea in mind, constant drainage was immediately started, accompanied by insulin, forced fluids, and a low protein high carbohydrate diet The patient im-

proved immediately, and in three days the blood sugar concentration was 270 mgm and the urea nitrogen concentration 10 mgm per 100 c c of blood The temperature dropped from 100 2° to 98 6° F The patient soon had a suprapubic prostatectomy performed under gas-oxygen anesthesia, and eventually left the hospital in excellent condition

The enlarged prostate with resultant retention of urine was the most important factor in the production of coma in this case The clinical picture might have been confused with that of diabetic coma The high alkali reserve of the plasma, coupled with the negative ferric chlorid reaction of the urine, combined to exclude diabetes as the cause of the coma The use of insulin influenced favorably the subsequent progress of the case and enabled the performance of a successful operation

CONCLUSIONS

The cases allow in conclusion a few general remarks about diabetes and coma

The onset of acidosis with resulting coma may be very acute and may be precipitated by an infection, by gross dietary indiscretions, or by failure to follow out the details of diabetic treatment

The CO_2 combining power of the blood is a better indicator of the degree of acidosis than is the urinary diacetic acid reaction The recent work of Bock, Field and Adair, of Starr and Fitz, and of others suggests that other acids than the ketones may help to produce acidosis in diabetes This fact probably explains the small amount of diacetic acid demonstrable in the urine of certain of the cases with severe acidosis It is important to know whether or not alkali has been administered in those cases in which the CO_2 combining power of the blood and the diacetic excretion in the urine are both high, and it is dangerous to make the diagnosis of diabetic coma in cases without a lowered alkali reserve

There is usually a relatively high red and white blood-count in coma cases The blood-changes are probably due to the dehydration, which may be marked in acidosis

The successful treatment of diabetes requires rigid attention to details on the part of the patient in regard to diet and personal hygiene He must learn what to expect if he does not observe the rules of treatment and if he does not keep his urine sugar free Since the introduction of insulin in the treatment of diabetes deaths from this disease and from the resulting acidosis have undoubtedly diminished The figures of the Metropolitan Life Insurance Company, calculated up to November 15, 1924, and published in their Statistical Bulletin in New York, show a decrease of 11 4 per cent in deaths from diabetes over that of the preceding year These facts must not lead to carelessness in regard to diet and the other details of treatment on the part of insulin users, but rather should stimulate even greater care than ever before because of the prospect of added years and economic efficiency

Finally, it is not out of place to emphasize a few practical details which may be of value in managing a case of diabetes with severe acidosis or in coma

1 Obtain a sample of urine and examine it for sugar and diacetic acid at the earliest possible moment (This may easily be done in the home if small vials of the necessary reagents are always carried)

2 If large amounts of sugar and of diacetic acid are present treatment for diabetic acidosis should be started immediately, regardless of the presence of complications

3 Treatment should not be put off until a patient can be taken to a hospital, as this may cause several hours delay The patient should be placed in a warm bed with means of keeping it warm An enema should be given Fluids should be given by every possible means In the early stages of coma the patient can usually be aroused enough to take small amounts of fluid by mouth Small rectal injections are easily given in most cases with simple home apparatus Insulin should be given subcutaneously, beginning with 10 to 20 units, depending upon the amount of sugar and diacetic acid found in the urine The effect of insulin can be safely observed by repeated urine

analyses Blood tests, though desirable, are by no means necessary

4 The burden of the diagnosis and treatment of diabetic coma rests with the physician who is first called in to see the case All doctors should be familiar with the clinical picture of diabetic coma and should carry an ampule of insulin as part of their emergency kit

CLINIC OF DR FRITZ B TALBOT

MASSACHUSETTS GENERAL HOSPITAL

ACUTE RESPIRATORY INFECTION WITH GASTRO-INTESTINAL SYMPTOMS

THE following case is an example of a condition frequently met in private practice, and less often in hospital practice, except in the later stages of the disease It is presented to illustrate the principles on which treatment is based and to give an example of the method of treatment used in the Massachusetts General Hospital

E M , girl aged thirteen years had been perfectly well up to the morning of December 25th when she commenced to vomit and to have diarrhea Between 4 and 10 A M she had vomited half a dozen times complained of intense pain in the bowels, and had very profuse watery stools with considerable gas, after which the abdominal pain was relieved Her appendix had been removed several years before and there was no history of indiscretions of diet

Her physical examination showed a sick pale-looking child, with a temperature of 99° F The throat, aside from considerable reddening and an edematous uvula, was normal The abdomen contained considerable gas and was slightly tender to palpation, especially over the colon There were no masses or spasm Otherwise the physical examination was normal

The following day she had ceased to vomit and the diarrhea was less severe She apparently was better but complained of feeling weak and had no appetite The diet was composed chiefly of cereals without milk Large amounts of water were taken in all at least $2\frac{1}{2}$ quarts in twenty-four hours She continued to improve except for a hacking cough Three other members of the family at approximately the same time had similar attacks of what was considered abdominal grip

The onset of symptoms is usually marked by vomiting or diarrhea and occasionally an elevation of temperature, which may go as high as 103° F on the second or third day During the period of gastro-intestinal symptoms the child looks extremely sick Later a cough may appear and last anywhere from several days to two or three weeks There may be a recurrence of symptoms within two to four weeks if the necessary precautions of rest and diet are not observed during convalescence

It is possible to diagnose this condition with a fair amount of accuracy A general physical examination should, however, be made to rule out other causes of vomiting and diarrhea, such as meningitis, encephalitis, nephritis, appendicitis, and other surgical abdominal conditions After ten years of age the occurrence of recurrent or cyclic vomiting is relatively rare

A negative physical examination, aside from the slight reddening of the throat, rules out infectious diseases which commence with vomiting, and leaves by elimination the diagnosis of abdominal grip or nasopharyngeal infection with gastro-intestinal symptoms This diagnosis, of course, is not scientific, but is common parlance at the present time

The treatment is of great importance both for the comfort of the patient and for the outcome of the disease Early treatment depends upon two general principles—sufficient water should be given to maintain the body fluids, and when food is given it should be selected so as to counteract a ketosis

The fluid intake should be carefully recorded and summed up at the end of twenty-four hours An infant of one year who has no diarrhea should receive at least 1 quart of fluid in twenty-four hours Small amounts, 1 tablespoonful at a time, are usually taken with impunity, whereas larger amounts, 2 or 3 ounces, if given at one time, are frequently vomited After sufficient fluid has been retained for three or four hours without vomiting the amounts may be rapidly increased If sufficient fluid is not retained by stomach it may be introduced very slowly into the rectum A warm normal saline solution containing 5 per cent glucose run in drop by drop is a very satisfactory means of accomplishing this In this way as much as 10 or 15

ounces may be retained in an hour In order to rest the rectum a lapse of two or three hours is necessary before another administration

When vomiting and diarrhea are present it is impossible to use this means of introducing fluid If dehydration is present a normal salt solution should be given subcutaneously This is an effective means of treatment, and makes it possible to maintain the body fluids even though no liquid is retained by mouth or rectum

When the vomiting is self-limited carbohydrate in the form of cereal gruels or jellies, without milk and with a small amount of sugar, may be given, 1 to 2 tablespoonfuls every two to three hours

The diet may be gradually increased during convalescence, cereals without cow's milk, orange juice, rice, crackers, and clear jellies To these may be added, a day or two later, broths, skimmed milk, and green vegetables, slowly increasing to meats, potato, apple sauce, simple desserts without milk, and butter, until a full diet is reached

Cow's milk is usually not well borne in these cases until the stomach has been settled for several hours Some form of malted milk, which is principally sugar, may be given earlier, and is usually well tolerated Later skimmed cow's milk may be given, the fat in whole milk often upsetting the digestion and causing a recurrence of vomiting

In cases of severe or persistent vomiting either hot or cold water in small amounts frequently given often relieves the retching In other instances temporary complete abstinence of everything by mouth is helpful Very few drugs seem to affect the vomiting Occasionally cocain, grain $\frac{1}{4}$, milk of magnesia, 1 ounce, soothe the stomach temporarily when given in teaspoonful doses

If the vomiting persists the alkali reserve of the body becomes lowered and the added complication of a fasting acidosis must be considered When this occurs sugar should be introduced by rectum, and in more severe cases either subcutaneously or intravenously In this way the ketone acids in the body are

reduced and bicarbonate of soda set free for its normal uses The use of bicarbonate of soda as a therapeutic measure has frequently been overdone in the past, occasionally with tragic results, an overdose causing alkalosis with convulsions, edema, and even death It has been found that it is rarely necessary when enough carbohydrate is retained in the body The younger the patient, the greater the susceptibility to alkalosis, and, consequently, the greater the dangers from the use of soda More than 2 teaspoonfuls of soda in twenty-four hours should not be given to any child In fact, it is frequently unsafe to give an infant more than a total of 2 teaspoonfuls during an illness Glucose, on the other hand, rarely causes untoward symptoms, but, like all therapeutic measures, should be administered with care and not to excess

The form of sugar used should be as nearly as possible the same as that found in the blood, that is, chemically pure dextrose The commercial form of dextrose (glucose) should not be used intravenously because of the possible presence of acids, such as sulphuric acid Chemically pure glucose or dextrose is usually given subcutaneously or intravenously in a 10 per cent solution, and should be freshly prepared and sterile and buffer salts added Buffer salts, as recommended by Stoddard,[1] should always be employed when intravenous injections are used

It should be remembered that fasting is a frequent complication in the infections of childhood and the principles underlying its treatment borne in mind If a child fasts for more than twenty-four hours the glycogen reserve of the body is lowered and the energy supplied by the body fat In order that there may be complete combustion of fat there must be an available supply of carbohydrate This, in all probability, is obtained from the body protein, but only in amounts sufficient to prevent an excessive formation of ketones The ketones include acetone, diacetic and beta-oxybutyric, the latter two being acids These acids combine with the bicarbonate of the blood and a lowered alkaline reserve results So long as enough alkali remains to

[1] Stoddard, James L , The Avoidance of Intravenous Glucose Reactions, Boston Med and Surg Jour , 1924, 191, 1121, No 24

carry off the carbonic acid and other normal acids of the body there is a compensated acidosis which does not require treatment If the acidosis becomes uncompensated, symptoms of a severe acidosis appear, with air-hunger and cherry red lips This is not an unusual complication of prolonged vomiting

If the necessary precautions as regards treatment, proper diet, the maintenance of body fluids, and the prevention of anhydremia are taken, the patient recovers rapidly unless there is an underlying complication of septicemia or some similar disease, as pneumonia.

CLINIC OF DR GERALD BLAKE

Massachusetts General Hospital

PTOSIS—OPERATED

The patient, an unmarried woman thirty years old, who had been a schoolteacher, entered the hospital April 8, 1923, complaining of nausea and vomiting, together with pain in epigastrium and right shoulder The present attack had been of eight weeks' duration and was similar in character to the attacks she had experienced since childhood, in which the above symptoms were associated with a variable amount of diarrhea, alternating with periods of constipation She gave the following operative history

Appendectomy, 1909, adhesions, 1917, cholecystostomy, January, 1919, cholecystectomy, November, 1920, gastroenterostomy, August, 1921, and in 1923 she complained of the same symptoms from which she had suffered before the first operation

Admitted to the hospital for study The wise and natural conclusions of the surgeon on whose service she was placed was that she should have no more surgery His note reads "Her general appearance fairly good in spite of long history Characteristic thing in regard to her attacks is that they have not been modified, or only temporarily modified, by the operative procedures It seems logical to suppose that further operation will be followed by no better results I can find no definite basis for exploration Her tenderness seems to me to be more psychic than real"

Physical examination showed a tall, thin, fairly nourished woman, showing no obvious pathology in the head or thorax The abdomen showed scars of operations, and the wall was

held very rigid Slight pressure everywhere seemed to excite pain which was referred to the scars No masses were felt There was no visible peristalsis *x*-Ray of the chest was negative Gastro-intestinal *x*-ray showed the stomach to be extremely low and atonic, but emptied in normal time On giving a second barium meal, it was seen to pass out of the stomach with usual rapidity by way of what appeared to be a gastro-intestinal anastomosis behind the greater curvature Nothing passed the pylorus The ileum was low and nearly empty at six hours At six hours the barium had passed splenic flexure Cecum and colon not remarkable, except for low position General abdominal tenderness present, but not localized to any special point The findings are those of posterior gastro-enterostomy functioning with unusual freedom There is marked visceroptosis and atony and very probable postoperative adhesions The blood showed nothing but a slight secondary anemia Examination of the stools was negative, except that twice mucus was found Gastric analysis showed the absence of free HCl and diminished total acidity in both the fasting stomach and test-meal examinations

The patient was put on a course of rest, with a high caloric diet, in the hope that her general muscular tone and weight could be improved to such an extent that she might be able to return to her work She co-operated to the best of her ability and was encouraged at the prospect of gaining strength by this method However, at the end of two weeks she found that the increased diet caused intense pain and she was unable to eat a sufficient amount The pain was fairly constant and prevented her sleeping It was not affected by bismuth or alkalies She began to lose weight steadily, and vomited much of the food eaten Under these circumstances operation was advised for the purpose of exploration, separation of adhesions, if found, and such other procedure as the surgeon thought indicated from his findings The intense pain had suggested the possibility of jejunal ulcer, and the vomiting indicated the presence of adhesions

At operation the stomach, transverse colon, and omentum

were found adherent to the abdominal wall. There was no evidence of constriction of the stomach or transverse colon by these adhesions On turning up the colon, a normal appearing gastro-enterostomy was exposed, the jejunum being somewhat large, and the stoma large enough to admit three fingers There was no evidence of kinking or inflammation The pyloric end of the stomach was densely adherent to the anterior abdominal wall and liver It was not possible to separate the adhesions and expose the pylorus The region of the gall-bladder and the common duct could not be exposed No induration was felt suggesting active ulceration Under these circumstances, since the pylorus had probably been closed by pervious operation, it was not possible to undo the gastro-enterostomy Partial closure of the stoma seemed of doubtful value After separating adhesions of the omentum, stomach, and heptic flexure from the abdominal wall, the wound was closed It seemed wise not to do anything which might intensify the symptoms The patient made an uneventful convalescence At the end of eleven days she complained of nothing She had no pain She had a good appetite and had regained some weight One questions how long this improvement will last

In the case described here we are dealing with a marked degree of ptosis—probably congenital, and probably incurable from the standpoint of entire relief of all symptoms Readjustment of viscera ptosed at birth is an impossibility Our attempt in such cases is to minimize symptoms resulting from such ptosis, and to promote the strength and health of the individual to the point where she can earn her living with comparative freedom from discomfort. If we cannot do this by the medical and orthopedic measures to be described we certainly cannot do it by surgery, and following the final surgical operation the patient returns to the physician for the best relief he can afford her along the lines to be described At that time her condition is as it was before, plus the mental and physical trauma of successive operations, and the additional adhesions resulting therefrom Obviously, where there has been acute inflammation in the peritoneal cavity, as from appendicitis and cholecystitis,

operation is necessary and should be performed In this case, however, it is not clear that at any time such an acute inflammation existed, and it seems probable that the operations were performed for symptoms due, in fact, to the ptsosis of the abdominal viscera She had to have her last operation because her health was impaired by the presence of adhesions which prevented the ingestion and assimilation of sufficient food, but that her relief is more than temporary is most unlikely The maximum effort to avoid this condition should have been made in her case before any surgery at all was performed

The medical and orthopedic treatment of ptosis depends for its success on two factors prescription of a correct regimen and constant conscientious carrying out of this régimen Even granted both these factors accomplished, it is by no means certain that complete relief of symptoms will be obtained, but improvement may fairly be looked for and marked relief expected in most cases The ptotic régimen includes careful direction of diet, regularization of the bowels, exercises to strengthen the muscles of the abdominal wall and intestinal tract, and sufficient efficient support of the abdominal wall until such time as the muscles themselves can do their work satisfactorily

Food should be nourishing and taken in small amounts frequently rather than in large quantity three times a day The diet should be well balanced and contain a moderate amount of roughage A good rule is to limit the liquid taken at any one time to 8 ounces for the same reason that small amounts of food are desirable, to permit easy and normal rapid passage through the ptosed stomach The patient should rest lying down after each of the three larger meals of the day, and a short rest before these meals is also advantageous If the indigestible foods are avoided and requisite amount of calories are provided, the variety of food need not be restricted Our experience has been that these patients, as a rule, limit their diet unnecessarily Milk is useful as an aid in bringing up total calories

Regularity of defecation should be brought about by the use of mineral oil or agar, or both these aids, and sufficient fruit

and green vegetables should be included in the diet to gain the effect of the fruit juices and roughage If difficulty is experienced in spite of these measures, enemata are preferable to the use of any cathartic drug

Exercises for developing abdominal muscles include deep breathing exercises, bending exercises, flexion of trunk on thighs, and thighs on trunk, etc, which are best performed morning and night Correction of faulty posture is an aid in improving the tone of these muscles Where active exercise is contraindicated or impossible, massage is of value

The need of support will depend somewhat on the age and musculature of the individual, it being obvious that older and thinner patients will require more support over a longer period than a younger or more robust patient A well-fitting corset, which holds the lower abdomen in and permits free use of the diaphragm, is indispensable This should be correctly adjusted, and is often best put on when the patient is lying in bed, at which time the lower half of the corset can be correctly adjusted No corset or support will do all that it is intended to do in holding the abdominal viscera in place, but a great deal may be accomplished by the careful fitting and careful daily adjustment of the correct corset The use of such support at the same time that exercises are being performed for strengthening the very muscles the corset supports is not inconsistent In daily life there are long stretches in which the abdominal muscles are not exercised, and it is precisely during these times that support is most necessary It is particularly true that with this type of patient the road to improvement is a long one, with need of all possible assistance along the way to accomplish the desired result It must be borne in mind that following necessary or unnecessary surgery these cases of ptosis return eventually to the form of treatment outlined above if they are to obtain moderate degree of relief of their symptoms Indications for surgery in cases of marked ptosis should be limited to (1) the presence of acute inflammation in the peritoneum, (2) when in spite of careful and correct medical and orthopedic treatment the patient continues to lose weight, or to suffer crippling pain,

for which no other cause can be found, and for which medical treatment has been unavailing, the possibility of hidden malignancy or operable adhesions make operation for these cases desirable

A CASE OF STREPTOCOCCUS SEPTICEMIA TREATED BY INTRAVENOUS MEDICATION

THE patient, a thin, nervous shoolgirl thirteen years of age, entered the hospital July 13, 1924, complaining of pain in the back of the head and bad feeling all over Temperature was 103 5° F She had been sick in bed ten days, during all of which time she had fever sometimes reaching 104° F , and pain in occipital region and under the left ear Eight days before entrance she had a chill and has had one each day since Six days ago there was definite injection of the left ear drum, with slight bulging Paracentesis was not thought necessary, and not done, and the inflammation subsided in two days For the past week she had pain in the back, the feet, and some of the other joints Three days ago and two days ago she vomited everything eaten

Past history was unimportant except for the occurrence of frequent colds and tonsillitis previous to tonsillectomy in 1921 Patient also gave history of pain in the right ear one year ago

Physical examination at entrance showed a flushed, restless child, difficult to talk to The pupils were equal and reacted The throat was negative The ears were negative The heart was rapid, but otherwise normal The lungs were clear Abdomen was negative except for general hypersensitiveness There was moderate stiffiness of the neck A double Kernig was present, apparently influenced by pain in the hip-joints No other change in reflexes White blood-corpuscles 20,000 The urine contained much epithelium and some pus-cells The spinal fluid was negative, showed 6 cells, but no other abnormality Widal was negative Blood-culture showed Streptococcus hemolyticus Blood-smear was negative

During the first two or three days the meningeal symptoms increased and lumbar puncture was repeated The spinal fluid was again negative Fundi normal There was slight tenderness under the left ear, which appeared to be of the

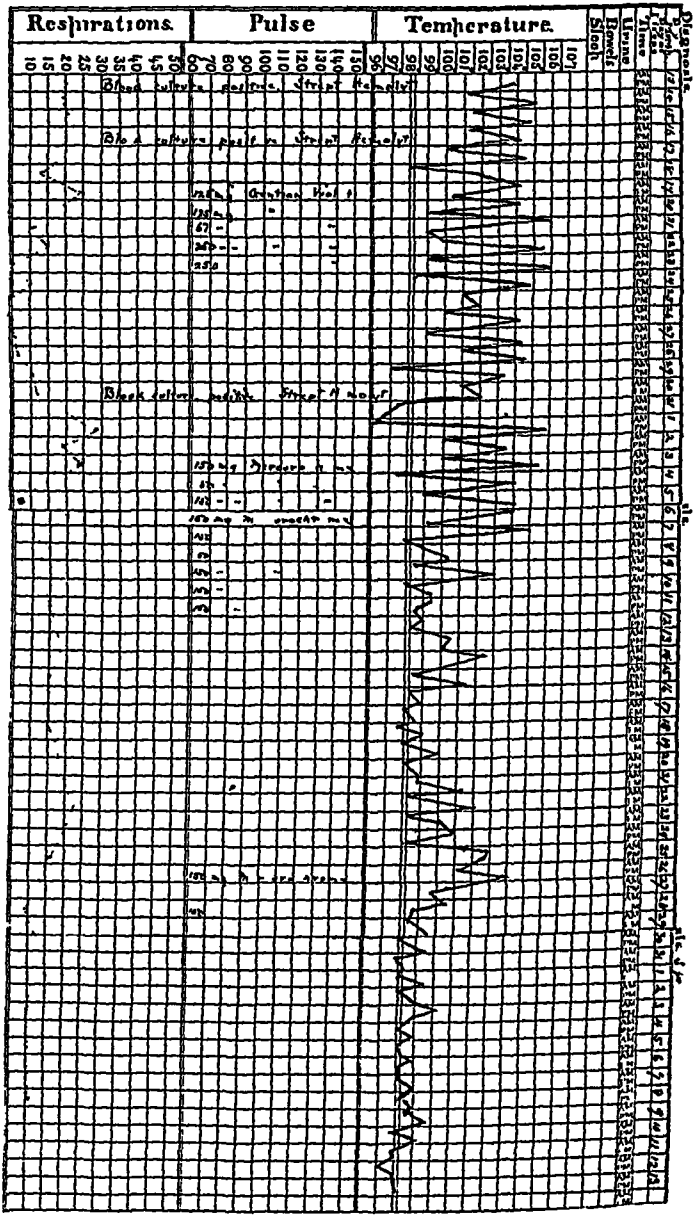

Fig 232.—Streptococcus hemolyticus septicemia Temperatures shown are the highest and the lowest in each twenty four hours Lower curve is that of the white blood count

muscles rather than from mastoid area Examination of the ear showed no evidence of active inflammation *x*-Ray showed some old destruction of mastoid wall on the left, but no activity was apparent The course of the case is sufficiently described by the temperature chart appended Intravenous medication was tried because of the fact that the child was desperately sick and appeared to be losing ground Because of her slight physique and stature treatment was first started with one-half the usual dose of gentian-violet, but the fourth and fifth injections were full doses Gentian-violet was then discontinued because of difficulty from blocking of the veins following these injections As there appeared definite improvement in the patient's condition, no further intravenous medication was given for eleven days, at which time a lighting up of the process, with marked access of fever and increase in the white count, made further treatment seem indicated Mercurochrome was then used for a series of nine doses, and was then discontinued because of improvement in the patient's condition and because of the appearance of purplish-red areas between the teeth and general spongy appearance of the gums After an interval of fifteen days two doses of mercurochrome were administered, with one day between, and following this further medication was unnecessary, the patient making a good recovery Since leaving the hospital she has gained between 15 and 20 pounds in weight, and has shown no sequelæ of her septicemia

This case is shown merely as a case of hemolytic streptococcus septicemia which was treated with gentian-violet and mercurochrome and recovered This type of case may recover anyway, and it may be that the intravenous medication had no bearing on the final outcome Two facts were noticable, however, and worthy of record First, the change in appearance following the second injection of gentian-violet, at which time it was observed that, although still desperately sick, she appeared less restless, less prostrated, and suggested more resistance to the disease than she had hitherto shown Second, the striking drop in the white count following the first injections of gentian-violet and of mercurochrome

It is to be considered whether the drying up of the original focus of infection—probably inflammation of the left middle ear—did not aid in permitting the maximum effect of the bactericidal agents on the organisms in the blood-stream, the more so, since experience has shown that in surgical septicemia where an infected area is constantly feeding the blood-stream the results of this treatment have been generally unsatisfactory I am impressed with the fact that this child was a poor risk, physically below par, and unstable nervously, obviously her mental and physical resistance to disease were both low She showed the first signs of improvement following her injection, and on this basis I would try this treatment on a similar case in the future

"INTESTINAL INFLUENZA"

A SINGLE woman, thirty-eight years old, entered the hospital September 10, 1924, complaining of cramps and gas in the stomach, which began one week before entrance, at the time of her return from a trip to West Virginia Her past history was of interest because she was said to have had typhoid fever in 1904, and an attack of anemia in 1919, which lasted for six months The anemia cleared up following the use of pills taken by mouth In 1920 she had influenza She had never been strong and got tired easily, but had always been able to carry on her work, which was that of a housekeeper Her color had never been good, but there was no history of bleeding or bruising easily, nor had she observed spots on the skin at any time There had been no previous diarrhea or constipation She entered the hospital on the recommendation of her physician, who considered that she might have primary anemia

One week before entrance she was taken quite suddenly with cramp like pains in the abdomen, mostly to the left of the umbilicus These continued for thirty-six hours, during which time there were eight watery dejections, normal in color She experienced slight chills followed by occasional sweating, severe occipital headache, weakness and malaise, and had run a temperature from 101° to 102° F for the four days previous to admission At entrance her temperature was 102 5° F , pulse, 110, respiration, 16 She continued to run a temperature of 100° F for the first six days in the hospital, following which it gradually dropped to normal The pulse varied between 110 and 80, and finally remained at the lower figure

Physical examination was almost entirely negative She had a slight secondary anemia Her white count at entrance was 4400 Widal was negative, both to Bacillus typhosis and to B paratyphosis A and B There was no growth from the stools in five examinations The urine was normal The

blood-culture showed no growth During the first week in the hospital the patient complained of extreme weakness, pain and discomfort in the head, back and limbs, and indefinite lower abdominal pain, which was intermittent, and some inability to sleep because of her general discomfort During the second week in the hospital most of these symptoms disappeared, but her weakness persisted to a marked degree, and there was much mental depression because of lack of strength At the end of the second week, however, she was able to go to a Convalescent Home, and finally made a complete recovery

This patient presented a picture similar to that of the milder cases of acute infection affecting the intestinal tract seen so commonly during the pandemic of 1918 and 1919 As in the other manifestations of the disease (influenza), the striking characteristics were the prostration, malaise, and often extreme toxemia which frequently gave rise to symptoms suggesting inflammation in the peritoneal cavity With the subsidence of the pandemic the severe cases have been infrequently seen, but a mild form of the same symptom complex has appeared with varying frequency since 1919 During the fall months of 1924 the condition had reached almost epidemic proportions in certain parts of Massachusetts The case cited is fairly typical of this group a sudden onset, with diarrhea and cramp-like pain in the lower abdomen, chills and chilliness, with fever, prostration, aching of the head, back and limbs, loss of appetite, and the protracted convalescence apparently out of proportion to the severity of the original infection In many instances there is seen at onset an inflammation of the lymphoid tissue at the sides of the pharyngeal wall which persists for two or three days without local subjective symptoms This probably marks the place of entry of the infectious agent A low white blood-count is generally found The pulse-rate is usually not much increased In severe cases tenderness and spasm over the whole abdomen, or in certain areas of the abdomen, may be observed, and this gives rise to the question of the presence of peritonitis One case observed in which the spasm was marked in the right lower quadrant came to operation six months later

during an attack of acute appendicitis At operation no evidence of old inflammation in or around the appendix was found The term "intestinal influenza" is an unsatisfactory one, especially at this time, when the definite symptoms so commonly seen during a pandemic have become modified and attenuated We have, however, no better terminology to characterize the condition It is a toxic diarrhea due apparently to the same organisms that cause the affections of the upper respiratory and respiratory tract, and also the stomach and liver The widely observed infectious catarrhal jaundice is a manifestation of the same infection localizing in a different area

While some of these cases show symptoms of gastric disturbance, it is the exception rather than the rule that nausea and vomiting occur in those individuals who have intestinal symptoms It is true, however, that cases showing purely gastric disturbances, without intestinal symptoms, frequently occur at the same time the intestinal cases are prevalent

Differential diagnosis at the height of the attack usually includes food-poisoning, peritonitis in the right lower quadrant or pelvis, typhoid fever, toxic diarrhea, or so-called "intestinal influenza" or "intestinal grippe ' Food-poisoning seldom presents the rise in temperature seen in these cases and is usually associated with vomiting There is usually a history of some suspicious article of food taken, and the occurrence of similar attacks in other individuals who have partaken of the same food I have seen however, two or more members of one family affected by "intestinal grippe ' within twelve hours, and have been forced to reject diagnosis of food-poisoning by the course of the disease with continued fever, etc , together with freedom from symptoms of other members of the family who have eaten the same food as those affected Of importance in ruling out peritonitis is the low white count, the rapid subsidence of pain and localized spasm, and the rare occurrence of nausea and vomiting in this group of cases It is true, however, that evidence of spasm may be so marked as to induce surgical interference for fear of overlooking an early inflammation in the peritoneum It seems to me that the low white count in the presence of the

well-marked rise in temperature is a valuable point for consideration Typhoid fever, especially in persons who have been vaccinated more than two years previously, is difficult to rule out at the time of the initial temperature The manifestations of typhoid may be very much modified in the patients who have been vaccinated from three to eight years before the attack, and it is frequently only by blood-culture that the diagnosis can be positively made Widal reactions appear not to be dependable The absence of rose spots and the very transient enlargement of the spleen are noticeable, and fever of great intensity and short duration, falling almost by crisis at the end of five or eight days, may occur—also a more prolonged fever of less intensity The picture of typhoid in such individuals is distinctly atypical We must, therefore, depend largely upon a negative blood-culture or upon a mild progress and rapid clearing up of the attack Careful examination of a fresh stool will often reveal the presence of typhoid in obscure cases

The treatment of intestinal influenza consists in rest, promotion of elimination of the toxins by water, etc, support of the patient's strength, control of symptoms causing the discomfort, and attention to the problems of a satisfactory convalescence There is no objection to the use of salicylates for the relief of pain in the early days of the disease Diarrhea should not be arrested unless it persists, and then only after preliminary purging, preferably by castor oil As a rule, the diarrhea subsides when the toxic agent has lost its virulency through the use of forced fluids and the lapse of time Should it continue, however, to the point of weakening the patient, opium in some form will usually control it without detriment to the progress of the case And once the diarrhea is stopped, and evidence of toxemia diminished, the diet may be enlarged rapidly without fear of recurrence of this annoying symptom Support of the patient's strength is then indicated, and a general high caloric diet is of importance in attaining this In respect to a satisfactory convalescence, sufficient rest appears to be primary in importance It is not uncommon to see the debility following the attack unnecessarily prolonged by too quick return to the

usual routine of life The prognosis is unqualifiedly good once the diagnosis is correctly made With the increase in typhoid fever, partly to be accounted for by the loss of immunity in a great number of individuals vaccinated during the time of the war, it is important that this possibility should be borne in mind in every individual case

CLINIC OF DR THOMAS E BUCKMAN

BOSTON CITY HOSPITAL

SPLENOMEGALY IN INFANTS AND CHILDREN

Four General Types of Splenomegaly I Splenomegaly Associated with Infections II Tumors III Hypersplenism IV Splenic Anemia

GENTLEMEN Though the causes of enlarged spleen in early life are numerous, it is possible to group most of these under the four main headings mentioned above At the outset I should like to point out that an enlarged spleen frequently does not have the same significance in early life that it does in adults A palpable spleen in an adult is nearly always evidence of serious disease, a palpable spleen in an infant or young child may be a sign of serious disturbance, but is frequently encountered in benign conditions

In the present state of our knowledge an etiologic classification of the causes of splenic enlargement is impossible Such a classification would be desirable, but is not absolutely necessary for the purposes of clinical analysis That is, splenomegaly is a physical sign, like edema, which we should like to be able to explain in every instance but which we are frequently unable to explain Inasmuch as splenectomy often gives temporary if not permanent relief in many cases, it is really more important to learn how to decide what type of case will be benefited by the procedure than it is to affix a name to the condition in the form of a diagnosis

We have to consider this morning 4 cases illustrating the principal types of splenomegaly.

Case I—A H, male, eighteen months old The family history is negative He was born at full term and nursed for six months He was then given whole milk and water with added sugar until about ten months of age Since then he has had, in addition to whole milk, cereals, beef juice, and eggs, but no green vegetables Eggs were added to the diet about two months ago Six weeks ago, at the age of sixteen and a half months, he weighed 26 pounds Except for the fact that he has always been rather pale he has not been sick Six weeks ago he had measles, which was followed by pneumonia During the course of the pneumonia it was noticed that the spleen became enlarged, so that its lower border extended to a level 4 cm below the costal margin in the nipple line The organ was soft and non-tender It had not been palpable before The lower edge of the liver was palpable Otherwise the physical examination was negative except for the signs in the lungs and slight epiphyseal enlargement at the wrists Today, after recovery from pneumonia, the physical examination is negative except for the palpable liver edge and the signs of mild rickets The spleen cannot be felt

Throughout the course of the pneumonia the blood showed very interesting changes which are summarized below

October 18th About four days after onset of pneumonia patient acutely sick Marked cyanosis Râles throughout both sides of chest back and front Signs of consolidation at the left base behind and over the middle lobe of the right lung Lower border of spleen palpable 6 cm below costal margin in nipple line—soft and not tender

Temperature 104 6° F, pulse, 140, respiration, 48

Examination of the Blood—Hbn, 70 per cent Red cell count, 4,800,000 White cell count, 84,000 Percentage of reticulated red cells, 8 Platelet count, 900,000 Differential count of 400 leukocytes

Examination of the stained specimen showed marked variations in the size and shape of the red cells There were many schistocytes among the red cells Basophilic stippling was a prominent feature, the granules being both fine and coarse

	Per cent	Total
Old polymorphonuclear neutrophils	59	49 900
Young polymorphonuclear neutrophils	12	10,100
Eosinophils	1	850
Mast-cells	0 5	450
Metamyelocytes	3	2,500
Premyelocytes	1	850
Myelocytes	4	3,400
Myeloblasts	1	850
Endothelial cells	7 5	6,350
Lymphocytes	11	9,300
	100 0	84,500

Numerous Cabot rings and Howell-Jolly bodies were seen The number of reticulated red cells was markedly increased

There was an obvious leukocytosis and though many young leukocytes were seen, there were no atypical or sport cells

The platelets were markedly increased in numbers and some of them were very large Rarely fragments of a megakaryocyte nucleus could be seen

I have had made a drawing of a typical field of a stained specimen of this blood, and now present this for your inspection

During the next ten days the patient was extremely sick, the temperature ranging from 102° to 104° F, cyanosis and marked prostration being features, the white cell count varying from 60,000 to 80,000 per cubic millimeter of blood The spleen continued enlarged Thereafter the patient gradually grew better the disease declining by lysis so that twenty-one days after the onset the temperature, pulse, and respirations were normal There was a slight exacerbation five days ago, but he has now apparently recovered

Discussion —The remarkable feature of this case is of course, the reaction of the hemopoietic system Marked leukocytosis with or without splenomegaly is not an uncommon finding in acute infections in early life Nor is it unusual to see immature red cells and immature white cells in the blood Such a marked reaction is not a common occurrence It is seen most frequently in pneumonia, though the same qualitative picture may occur in any acute infection in early life

A STUDENT What type of pneumonia did this infant have?

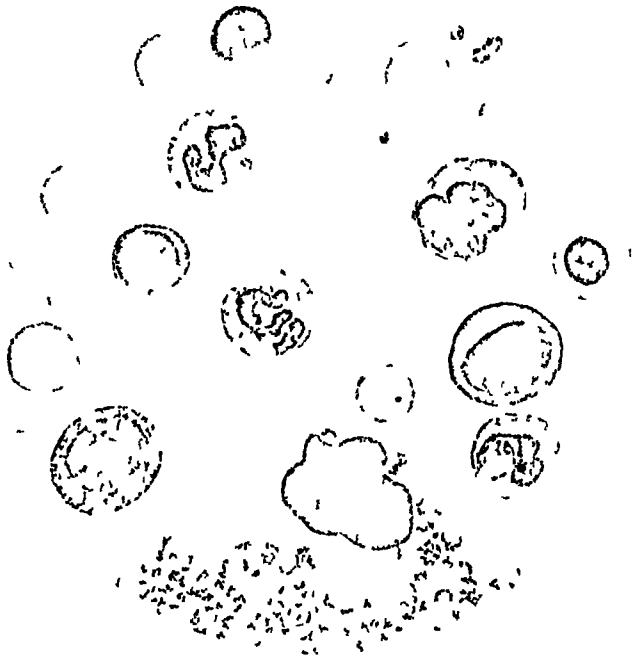

Fig 233 —Case I Camera lucida drawing of actual field of blood film Magnification ca 980

Interpretation —The large cell above the mass of platelets at the bottom of the drawing is the nuclear fragment of a megakaryocyte Above this and somewhat to the right is a red cell containing a Cabot ring and a Howell Jolly body, presumably nuclear, remains To the right of this red cell is a large leukocyte with a sharply outlined nucleus surrounded by deeply staining, homogeneous cytoplasm This is a myeloblast To the right of this is an erythroblast and above is a metamyelocyte characterized by the granular nature of the cytoplasm and the indentation of the nucleus At the lower left margin is a younger myelocyte in which the nucleus shows no signs of lobulation

Note that there is an outpouring not only of myelogenous leukocytes but also of lymphocytes, a feature of the response of infantile blood to infection The red cells show some variation in size and shape, but the remarkable abnormality is the polychromasia which is seen in almost every red cell The picture indicates a marked but orderly stimulation of all the formed elements of the blood

DR BUCKMAN If you mean what type of pneumococcus was found, I confess that no attempt was made to determine it.

It is practically impossible to obtain sputum from an infant unless one inserts a catheter into the pharynx Moreover, it makes no difference what form of pneumococcus is found Antipneumococcus serum does no good in infants, so that typing is not necessary from a therapeutic point of view From a prognostic point of view the prognosis is more safely determined by a consideration of the history than of the type of pneumococcus found in the sputum This baby had what we should call a secondary pneumonia that is, a pneumonia following or occurring in the course of another disease, in this case measles Primary pneumonia comes out of a clear sky The former has a non-specific etiology, is usually lobular in type, and has a high mortality rate The latter is usually due to some form of pneumococcus, is usually lobar in type, and, unless complicated by other conditions, has a very low mortality rate in children

A STUDENT Can you rule out myelogenous leukemia from examination of the blood alone?

DR BUCKMAN No This blood specimen shows all the ear-marks of marrow stimulation excessive numbers of white cells with many of the youngest forms, immature red cells, vast numbers of platelets, and even megakaryocyte nuclei True, there are no abortive or atypical cells, but an orderly outpouring of leukocytes is not unknown in myelogenous leukemia Rather against leukemia is the large number of lymphocytes over 9000 per cubic millimeter of blood or about four times as many as normal at this age There is a lymphocytosis as well as a myelogenous leukocytosis This is characteristic of the reaction of infantile blood to severe acute infections In an adult suffering from pneumonia the leukocytosis is due almost entirely to the increase in myelogenous cells, in early life there is also a lymphocytosis Another feature of the infantile reaction is the increase in the number of endothelial cells

Myelogenous leukemia could not be excluded from examination of the blood alone, but the disease is exceedingly rare in childhood and almost unknown in infancy, though a similar condition myelogenous chloroma, is rarely seen Of course, the recovery of the patient shows that this was not leukemia

A STUDENT What is the significance of the abnormal red cells?

DR BUCKMAN That is a difficult question to answer Schistocytes usually indicate excessive blood destruction One sees them in pernicious anemia, hemolytic jaundice, polycythemia, and certain varieties of septic anemia They occur frequently in infantile blood when excessive blood destruction is not otherwise evidenced, as in nutritional anemia and anemia due to hemorrhage They occur also in severe acute infections in infants and young children. One can say only that disintegrating red cells and microcytes are frequently seen in early life, and that one cannot attribute to their presence the same clinical significance as in adults

Red cells showing reticulum and nuclei and fragments of nuclei—basophilic granules, Howell-Jolly bodies, Cabot ring forms, etc —are young cells, and may signify either a lowering of the marrow threshold or an actual stimulation of the marrow It is usually said that the infant's blood easily reverts to an embryonic type. This merely restates the facts From a teleologic point of view it is easy to see why, in infections, leukocytes should be called out in excessive numbers, but there is no apparent reason why platelets and red cells also should be implicated The truth of the matter is that marrow stimulation is not an absolutely specific thing After hemorrhage not only is there an outpouring of red cells and platelets but also of leukocytes, in polycythemia vera, although the red cells are principally stimulated, leukocytes and platelets also share in the process, in myelogenous leukemia one sees an excessive number of platelets and many immature red cells Delivery of red cells to the circulation has been shown to be determined by growth pressure within the marrow, and this pressure probably affects all the marrow elements to some extent The outpouring of cells into the peripheral blood is thus not the result of the absolutely specific stimulation of one element

A STUDENT What prognostic significance can be attached to the level of the white count in pneumonia in early life?

DR BUCKMAN In a general way the same significance as in

adults Leukopenia and hyperleukocytosis at any age especially leukopenia indicate, generally, an unfavorable prognosis, but it is true that in early life many cases of pneumonia with leukopenia or hyperleukocytosis terminate favorably

A STUDENT In this case what part did rickets play in the causation of the splenomegaly?

DR BUCKMAN It is impossible to say The spleen is usually enlarged in infants who suffer from severe anemia whatever the type Moreover, many if not most infants who suffer from severe and prolonged nutritional anemia are infants who have been deprived not only of iron but also of sunlight, and hence show evidence of rickets In other words, there may be a causal relationship between enlargement of the spleen and anemia *per se*, but, in spite of the frequency of their association, there is no conclusive evidence to show that rickets itself is the etiology of the splenomegaly seen in these cases

Now, infants who suffer from rickets are particularly prone to suffer from recurrent infections, especially infections of the respiratory tract Such infections are usually accompanied by a leukocytosis If anemia and splenomegaly, from whatever cause are also present we have then the syndrome known as von Jaksch's anemia I do not mean to imply that von Jaksch's anemia may not be an independent entity but it is practically impossible to differentiate this entity from the syndrome seen in rachitic, anemic infants who suffer from recurrent infections

In this particular case there was no anemia, the spleen was not enlarged before pneumonia developed, and it could not be felt after recovery from pneumonia I should say, therefore, that in this case, at any rate, the rickets had nothing to do with the enlargement of the spleen

If there are no other questions we shall proceed to the next case

Case II—J McQ Male Age ten and one-half years Both parents are well Two other children are well There has been no known exposure to tuberculosis He had chickenpox, measles, and scarlet fever before he was five years of age

Three years ago he had whooping-cough From all of these he recovered without complications

Except for the above infections he has always been well until the onset of the present illness He developed normally both mentally and physically, and has always played and carried on with other boys after the manner of a normal child

Present Illness—Six months ago he had an attack of tonsillitis during which the cervical lymph-nodes on both sides became enlarged and tender He was sick with tonsillitis for about a week, and then seemed to recover except that he has felt rather listless, and has noticed that though the cervical glands have diminished in size they persist definitely enlarged He thinks that he has been feverish at times during the past month He has had no other symptoms

Physical Examination—He is a well-nourished and well-developed boy, rather pale and apathetic The pharynx is normal The anterior cervical lymph-nodes on both sides are distinctly enlarged, especially on the left side, where at least six almond-sized discrete, firm, and slightly tender nodes are palpable Three pea-sized lymph-nodes can be felt in the left axilla and two much larger nodes in the right axilla The inguinal lymph-nodes are very much larger than normal and there is slight edema of the scrotum The lower border of the spleen is felt 6 cm below the costal margin in the nipple line The organ is firm and non-tender At the right base behind there are flatness and diminished tubular breathing Otherwise the physical examination is not remarkable

As you see him today, ten days later, the physical examination remains essentially as on admission, though additional laboratory evidence has accumulated which may help in making a diagnosis The temperature has ranged from 98° to 100 6° F, the pulse from 80 to 120, respirations from 20 to 26

A STUDENT What did the examination of the blood show?

DR BUCKMAN On admission the blood examination showed the following

Hbn, 80 per cent Red cell count, 4,200,000 Platelet

count, 420,000 White cell count, 14,000 Differential count of 400 leukocytes

	Per cent.	Total
Adult polymorphonuclear neutrophils	72	10,080
Young polymorphonuclear neutrophils	3 5	490
Eosinophils	4 0	560
Myelocytes	0 5	70
Endothelial cells	8 0	1,120
Lymphocytes	120	1,680
	100 0	14,000

Examination of the stained specimen showed slight stippling of the red cells No atypical forms of leukocytes were seen The platelets were abundant

The features of this blood are the leukocytosis with preponderance of polymorphonuclear neutrophils, and the increase in the numbers of eosinophils and of endothelial cells Note that there is no increase in the number of lymphocytes

A STUDENT Is not this the picture that is supposed to be diagnostic of Hodgkin's disease?

DR BUCKMAN Yes According to Bunting the presence of a leukocytosis with preponderance of polymorphonuclear neutrophils, and especially when this is accompanied by an increase in the number of eosinophils and endothelial cells without a concomitant increase in lymphocytes, is highly suggestive of Hodgkin's disease The picture is not absolutely pathognomonic, however, in children in whom chronic or recurrent infection may produce a similar blood-picture and also a generalized glandular enlargement, Nevertheless, in such cases, especially if the infection is tuberculous, a lymphocytosis with neutropenia is the rule

Shortly after admission an x-ray plate of the chest was taken This showed evidence of a small amount of fluid at the right base Otherwise the plate showed nothing abnormal About 100 c c of fluid were withdrawn from the chest for diagnostic purposes The laboratory report of the examination of this fluid was as follows

Color, brown, slightly turbid Specific gravity, 1 020 Albumin, 3 per cent Cell count, 1800

Differential count of 200 cells Lymphocytes, 85 per cent Polymorphonuclear cells, 12 per cent Eosinophils, 3 per cent

A specimen of the fluid was inoculated into a guinea-pig as a means of detecting tubercle bacilli

Reports of other laboratory examinations were as follows

Mantoux test 1–5000 negative 1–100 negative 1–50 negative

Examination of section of cervical gland showed evidence of chronic inflammation

Wassermann tests of blood of patient and both parents were negative

We thus have a case of generalized glandular enlargement with enlarged spleen showing a blood-picture consistent with Hodgkin's disease The diagnosis is not confirmed by the report of examination of a section of removed gland Moreover, the character of the fluid removed from the chest is unusual for this condition It has all the features of an inflammatory fluid

A STUDENT Could this be a case of glandular fever?

DR BUCKMAN Acute tonsillitis apparently followed by generalized glandular enlargement To that extent the condition is consistent with glandular fever or acute infectious mononucleosis, but in glandular fever the white count is much higher and the preponderating cell is the lymphocyte There is often a polycythemia too This boy has been sick too long Moreover, glandular fever would not account for an exudate in the chest Lymphatic leukemia might be thought of Chronic lymphatic leukemia, however, is rare at this age, and though a leukocytosis is not a *sine qua non* of the disease (aleukemic leukemia), it seems to me that the burden of proof would be placed on anyone who would make this diagnosis on the basis of a single blood examination in which no leukocytosis was demonstrable

A STUDENT Could not all the findings be explained on the basis of tuberculosis?

DR BUCKMAN Tuberculosis might produce just such a clinical picture Moreover, it is possible to have active tuberculosis and Hodgkin's disease in the same patient at the same

time, and the two diseases are often confused (Dorothy Reed type of Hodgkin's disease) Yet we do not like to make a diagnosis of tuberculosis in the face of a negative reaction to the intradermal injection of as much as 2 0 mgm of tuberculin Moreover, there is no history of exposure to tuberculosis, and except for the sign of fluid in the chest there is no evidence of pulmonary tuberculosis All of this does not of course, exclude tuberculosis, but that seems to me an unlikely diagnosis On the whole, I think that Hodgkin's disease is more nearly consistent with all the findings than anything else and I should proceed on this basis with respect to diagnosis and therapy It is to be remembered, however, that in children many cases showing over long periods of time a generalized glandular enlargement with splenomegaly and a slight leukocytosis turn out to be cases of a non-malignant type, the condition being the result of a chronic or recurrent non-specific infection As I have said, such cases most frequently show a preponderance of lymphocytes in the blood-film, but this is not necessarily the case This boy has been carefully and repeatedly examined for focal infection—teeth, nose, tonsils, sinuses—but nothing has been found

A STUDENT Does the clinical type of glandular enlargement help in making the diagnosis?

DR BUCKMAN To a limited extent only Very small, hard glands are frequently palpable in the neck and even in the axillæ of apparently normal individuals and the inguinal lymph-nodes are usually palpable in children The commonest cause of cervical adenomegaly in children is, of course an acute or recurrent non-specific inflammation of the region they drain—the pharynx In such cases the glands are usually discrete, firm, and tender Frequently they suppurate Next in order of frequency is tuberculosis If healing takes place without much secondary invasion these glands persist as hard masses If secondary infection occurs, suppuration is likely to occur, or if actual necrosis does not occur a matting together results In Hodgkin s disease the glands remain firm and discrete and practically never undergo suppuration

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acute bilateral otitis media requiring paracenteses tympanorum It was noticed during this sickness that he was jaundiced, and ever since this time he has seemed pale and occasionally has been slightly yellow, but the urine has never been abnormally colored and the stools have never been clay colored At five years of age he had scarlet fever, followed by another attack of acute bilateral otitis media He made an otherwise uneventful convalescence During this illness it was thought that he was somewhat paler and more yellow than usual

The boy was first seen by me eighteen months ago at the age of five and a half years The parents sought medical advice because of the story I have just recounted, and especially because during the six months following the attack of scarlet fever it was thought that he was "losing ground" He had seemed paler and more yellow than before He vomited occasionally Though always a bright infant, the parents thought that he had shown less physical vigor than a normal boy of his age would have shown

On his first visit he appeared as a well-developed and fairly well-nourished, rather listless, but by no means stupid infant The skin and sclerae were distinctly yellow, but the coloration was not very deep The mucous membranes were pale

The head was of normal shape Oral examination revealed nothing remarkable There was no adenopathy The abdomen was soft The lower edge of the liver was felt 3 cm below the costal margin The lower edge of the spleen was felt 6 cm below the costal margin in the nipple line It was firm and not tender The abdomen was otherwise negative The genitalia were normal Nothing abnormal could be made out about the heart and lungs The extremities showed no evidence of rickets There was no edema The tendon reflexes were equal and normal Temperature, 98 6° F , pulse, 90, respiration, 22

Discussion—DR BUCKMAN Given a history of attacks of jaundice, extending over a period of years, and a definitely enlarged spleen in a child seven years old with a physical examination otherwise negative, what diseases should be thought of as the most likely causes of the symptoms?

A STUDENT What can be said about the etiology of Hodgkin's disease?

DR BUCKMAN That is unknown It is held by some that a specific organism, an ameba, is responsible, but that belief has not received wide-spread acceptance Many writers are of the opinion that the disease is due to a living cause as yet undiscovered Most pathologists, I think, are of the opinion that Hodgkin's disease is a neoplasm related to lymphatic leukemia and lymphosarcoma The histologic appearances of lymph-nodes in the three conditions are very similar Generally the pathologic report returned in any one of the three is "lymphoblastoma" In distinguishing further, one must rely upon clinical findings, and, especially, on the blood

A STUDENT What will be the further course of events in this case, treated and untreated?

DR BUCKMAN Death in either case in from one to five years The only important form of treatment as yet introduced is irradiation treatment, whether by radium or by short or long wave-length *x*-rays Such treatment has a beneficial effect in that it reduces the size of the enlarged glands and thus relieves pressure symptoms, whether it has any other effect, whether it prolongs life or not, no one knows

A STUDENT Would splenectomy be contraindicated in this case?

DR BUCKMAN Most cases of Hodgkin's disease in whom splenectomy has been performed have died shortly after operation Occasionally one has survived

If there are no other questions we shall pass to the consideration of the next case

Case III.—I. S B Male, aged seven years The family history is negative Both parents are well This boy is the first and only child He was born at full term after a normal delivery and seemed normal in every way at birth He was not jaundiced He was breast fed for nine months He had no illness and seemed to develop normally until about three years of age At this time he had a very severe cold, followed by

many schistocytes There is marked variation in the intensity of staining and marked polychromasia There is a moderate degree of fine stippling Some of the cells show achromia, but this is not a feature The white cells show nothing remarkable The platelets are abundant

Wassermann tests on blood of both parents and patient were reported negative

Urine Specific gravity, 1 016, acid, albumin, 0, sugar, 0, bile, 0, sediment, negative

DR BUCKMAN The marked increase in the fragility of the red cells and the great increase in the number of reticulated red cells, together with the absence of bile in the urine, make it extremely likely that this was a case of hemolytic jaundice or acholuric jaundice, as it is sometimes called, of the acquired type There are no facts inconsistent with this diagnosis

Further Course—During the six months following the time at which he was first seen the patient grew worse He suffered from more severe and more frequent attacks of icterus, and he seemed to become more and more listless At this time the blood examination showed the following

Hbn , 50 per cent Red cell count, 2,800,000 Reticulated red cells 14 per cent

Fragility of red cells

	Patient's cells	Control's cells
Hemolysis begins,	0 56 per cent NaCl	0 42 per cent NaCl
Hemolysis complete,	0 40 per cent NaCl	0 32 per cent NaCl

It was considered that splenectomy offered the best hope for permanent relief He was given a transfusion of 300 c c of blood and the spleen was removed He made an uneventful recovery from the operation, and has remained well ever since, no further attack of jaundice having occurred Now, one year after operation, the blood examination shows the following

Hbn , 96 per cent Red cell count, 5,000,000 Reticulated red cells, 1 per cent

Resistance of red cells to hypotonic salt solution

A STUDENT Hemolytic icterus, syphilis, some form of cirrhosis of the liver or spleen

DR BUCKMAN Yes Other causes, such as recurrent inflammatory condition in the gall-bladder and ducts, might be thought of, but it is better, as a rule, first to consider the more common causes of a given syndrome What further diagnostic procedures would you suggest?

A STUDENT A Wassermann test of the blood of both parents and patient, and an examination of the patient's red cells, especially an estimation of the number of reticulated red cells and a determination of the resistance of the red cells to hypotonic sodium chlorid solution

DR BUCKMAN These tests were made as well as many others, and the reports are as follows

Blood Examination—Hbn , 55 per cent Red cell count, 3,000,000 Color index, 0 91 Percentage of reticulated red cells, 12 per cent

Fragility of red cells (*i e* , resistance to hypotonic salt solution)

	Patient s cells	Control s cells
Hemolysis begins,	0 72 per cent NaCl	0 42 per cent NaCl
Hemolysis complete,	0 32 per cent NaCl	0 30 per cent NaCl

Measure of serum pleiochromia

(1) Patient's serum requires 400 dilutions to reduce to colorless, with distilled water as a standard

(2) Control's serum requires 30 dilutions to reduce to colorless, with distilled water as a standard

Leukocyte count, 8400

Differential count of 200 leukocytes

	Per cent
Polymorphonuclear neutrophils	64
Lymphocytes	27
Eosinophils	1
Endothelial cells	8
	100

Platelet count, 340,000

Examination of Stained Specimen—The red cells show marked variations in size and shape There are many microcytes and

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	Patient's cells	Control's cells
Hemolysis begins,	0 40 per cent NaCl	0 40 per cent NaCl
Hemolysis complete,	0 30 per cent NaCl	0 28 per cent NaCl

White cell count, 9000
Differential count of 200 leukocytes

	Per cent
Polymorphonuclear neutrophils	62
Eosinophils	4
Lymphocytes	26
Endothelial cells	8
	100

Examination of stained specimen The red cells appear entirely normal No immature leukocytes are seen The platelets are abundant

As you see this boy today the physical examination is negative and he appears in every way as a normal child

Discussion—A STUDENT Were the symptoms of weakness, lassitude, etc, due to the jaundice or to the anemia?

DR BUCKMAN I think that most of the symptoms of this disease are due to the anemia rather than to the jaundice It is commonly said that patients suffering from hemolytic jaundice are rather "more jaundiced than sick" When blood destruction becomes excessive then the jaundice is apt to increase, not because there is obstruction, of course, but because the pigments produced from hemoglobin are formed more rapidly than they can be eliminated At the same time, unless the response of the marrow is sufficient to compensate for the blood destroyed, anemia results, and when the hemoglobin reaches a level below about 60 per cent a patient is apt to suffer from symptoms of anemia—dyspnea, palpitation, lassitude, weakness, edema, even, in severe cases

A STUDENT Why does bile never appear in the urine?

DR BUCKMAN It is found in the urine when the jaundice is extreme, but this is very rare It is said, of course, that bile is not formed rapidly enough, so that the amount in the blood exceeds the threshold of elimination of the kidneys The

urobilin output, in both urine and feces, however, as determined by the number of dilutions necessary to cause disappearance of the characteristic spectrum, is always excessive in this disease

A STUDENT Is there any important difference between the familial and the acquired type of hemolytic jaundice?

DR. BUCKMAN It is held by some writers that cases of the acquired type of the disease are usually more severe than those of the congenital type Some have tried to assign a different etiology to the two forms, pointing out the frequency of associated infection in acquired hemolytic jaundice Still others maintain that the two diseases are identical, the disease existing potentially in the brothers or sisters of the patient in whom the disease appears to have been acquired It is certainly true that there are many cases of the disease in which symptoms have been very slight or entirely wanting, and in which the diagnosis has been made only as the result of a careful routine examination

A STUDENT Does hemolytic jaundice bear any relation to pernicious anemia?

DR. BUCKMAN Both diseases are illustrations of what is generally called hemolytic anemia, that is, of anemia due to excessive blood destruction in contrast to anemia due to defective blood formation This is attested to by the histologic examination of the blood Moreover, one frequently sees cases of pernicious anemia that simulate hemolytic jaundice in that they show jaundice, increased fragility of the red cells, increased numbers of reticulated red cells, and splenomegaly Also these are the cases of pernicious anemia which are benefited most by splenectomy

But to say that this constitutes evidence that the two diseases are closely related would be like saying that because carbohydrate is useful in combating the acidosis seen in diabetes, as well as in the acidosis of starvation, these two conditions must be similar In certain cases of pernicious anemia and in hemolytic jaundice similar mechanisms may be at work, but pernicious anemia is an entity in itself, and its influence on the hemopoietic system is incidental, albeit, dramatic

A STUDENT Why should removal of the spleen influence hemolytic jaundice so favorably?

DR BUCKMAN Botazzo called the spleen a hemocatatonistic organ, that is, an organ that *prepares* blood, especially red cells, for destruction Under certain conditions—hemolytic jaundice, certain cases of pernicious anemia, erythremia—this function of the spleen is greatly augmented—hypersplenism So considered, hemolytic jaundice becomes "essential" hypersplenism in the sense that exophthalmic goiter is "essential" hyperthyroidism Now, it is generally believed that increased fragility of the red cells *in vitro* is indicative of increased susceptibility to destruction *in vivo* and that such increased fragility may be, and, in hemolytic jaundice, is conferred on the red cells by the spleen Hence removal of the spleen should diminish the fragility of the red cells and thus lead to lessened blood destruction, and this, in turn, should lead to a lessened tendency to jaundice That removal of the spleen does this has been shown by experience both in man and in animals

A STUDENT When should splenectomy be performed in hemolytic jaundice?

DR BUCKMAN The answer is problematic, and the question is settled in different clinics in different ways Mild cases of the disease may go through life or at least for many years without important symptoms It seems to me unwise to subject such patients to a major operation even though the mortality is small On the other hand, once the diagnosis is definitely established, I think operation should not be delayed in any case in which disabling symptoms persist or recur Splenectomy is the only treatment that is of any avail, and, though traces of the disturbance, slightly increased fragility of red cells, slightly increased percentage of reticulated red cells, may linger for many years afterward, removal of the spleen effects, substantially, a cure in most cases of the disease

Case IV —A K Male, six years of age Both parents are well Three other children are well One child died in infancy and one at the age of three of scarlet fever There has

been no known exposure to tuberculosis This patient had chickenpox at the age of four and scarlet fever about a year ago From both of these he made uneventful recoveries

Until six months ago he had been well except for mild attacks of jaundice which he had had since he was four years old These attacks would last from ten days to two weeks and would be accompanied occasionally by fever and vomiting Pain was never complained of About six months ago it was noticed that his abdomen was growing larger and that he was becoming very much paler About two months ago he became rather deeply jaundiced, and this persisted until about ten days ago, since when the jaundice has diminished somewhat During this last attack it was noticed for the first time that his stools were clay colored Tarry stools have never been noticed He has never vomited blood

Two weeks ago, on admission to the hospital, the physical examination showed a well-developed but rather thin boy, of normal mentality, but obviously sick The skin and scleræ were mildly jaundiced A few almond-sized lymph-nodes were palpable in the anterior cervical lymphatic chains Otherwise the examination of the head and neck was negative

There was a short systolic murmur heard over the apex-beat of the heart, but the heart was not enlarged and there was no murmur in diastole The lungs were normal The abdomen was large and signs of free fluid were made out The lower border of the spleen extended 8 cm below the costal margin in the nipple line The right margin extended to the midline of the abdomen The lower edge of the liver was felt 6 cm below the costal border There was no tenderness over either the spleen or the liver

The genitalia and extremities were normal There was no edema of dependent parts The tendon reflexes were equal and normal

Laboratory examinations gave the following evidence

Wassermann tests on blood of patient and both parents negative

Blood Histology—Hbn, 50 per cent Red cell count,

3,000,000 Color index, 0 82 Percentage of reticulated red cells, 2

Resistance of red cells to hypotonic salt solution

	Patient's cells	Control's cells
Hemolysis begins,	0 42 per cent NaCl	0 40 per cent NaCl
Hemolysis complete,	0 32 per cent NaCl	0 30 per cent NaCl

White cell count, 5400

Differential count of 200 leukocytes

	Per cent	Total
Polymorphonuclear neutrophils	52	2800
Lymphocytes	42	2275
Endothelial cells	6	325
	100	5400

Examination of Stained Blood-film—The red cells show marked edema There is a very slight variation in size and shape and there is some fine stippling One is not impressed, however, by any marked abnormality in the erythrocytes No erythroblasts are seen The white cells appear sparse and there is an obvious increase in the proportion of lymphocytes There are no abnormal leukocytes The platelets are abundant

Platelet count, 260,000
Bleeding time, eight minutes (Normal, not over three minutes)
Coagulation time, thirty minutes (Normal, not over fifteen minutes)
Fibrinolysis marked
Serum shows marked pleiochromia

Blood Chemistry—Whole blood cholesterol, 600 mgm per 100 c c

Urine—Specific gravity, 1 020, acid, albumin, 0, sugar, 0, bile present, sediment negative

Stool—Test for occult blood negative Bile present

Ascitic Fluid—Specific gravity, 1 012, albumin, 0 5 per cent, cell count, 100 (lymphocytes), bile present

With the evidence at hand a diagnosis of cirrhosis of the spleen was made and splenectomy advised The operation was performed two weeks ago Before operation the patient was

given a transfusion of 300 c c of blood He was also given an hour before operation by deep intramuscular injection 15 c c of a 30 per cent solution of sodium citrate

He made an uneventful recovery from the operation, and as you see him today he is well on the road of convalescence His jaundice has almost disappeared and there is no evidence of free fluid in the abdomen

Histologic examination of the spleen showed fibrosis

Today the blood examination showed the following Hbn , 80 per cent Red cell count, 4,800,000 Percentage of reticulated cells, 3 White cell count, 8600

Differential count of 200 leukocytes

	Per cent	Total
Polymorphonuclear neutrophils	66	5675
Lymphocytes	30	2580
Endothelial cells	4	345
	100	8600

Platelet count, 640,000

The stained blood-film showed marked polychromasia and numerous normoblasts The platelets were increased

Discussion—DR BUCKMAN What do you think was really the matter with this patient?

A STUDENT I suppose this started as an infection of the bile passages resulting in a biliary or Hanot's cirrhosis, which later led to cirrhosis of the spleen

DR BUCKMAN I should say that this would be the most likely description of the histogenesis of the disease Generally speaking, anything that causes cirrhosis of the liver will sooner or later cause cirrhosis of the spleen, and vice versa Moreover, whenever marked cirrhosis of the spleen occurs there results an anemia of the so-called secondary type (low color index), with a leukopenia due to a suppression of the myelogenous leukocytes Sometimes a slight diminution of the platelets (thrombopenia) also occurs In addition to its function as a blood-destroying organ the spleen seems to exert an influence on the bone-marrow At least, whenever the spleen becomes cirrhotic, anemia of the myelophthisic type is likely to occur

Then, too, cirrhosis of the spleen interferes with the portal circulation About one-third of the blood in the portal system is carried through the spleen, and when obstruction in that organ occurs there may result ascites and even varicosities, so that hematemesis and melena are not infrequent symptoms

A STUDENT In what, then, does a case like this differ from a case of Banti's disease?

DR BUCKMAN Only in origin, not in end-results What Banti originally described as an entity was a primary endophlebitis of the splenic veins This would lead to cirrhosis of the spleen and then to cirrhosis of the liver There would finally occur the characteristic anemia, on the one hand, and on the other, the symptoms and signs of portal obstruction True Banti's disease is very rare or, at least, very rarely diagnosed In most cases the patient is not seen until both liver and spleen are cirrhotic, and then differentiation is often impossible If there is a history of splenic enlargement over a long period of time before enlargement of the liver occurs one is inclined toward the belief that the condition originated in the spleen If, on the other hand, as in this case, there is a history of attacks of jaundice occurring over many years before important enlargement of the spleen appears, it seems only reasonable to assume that the process started in the liver

A STUDENT What is the prognosis in this case?

DR BUCKMAN Since he has cirrhosis of the liver the outlook is undoubtedly unfavorable But removal of the spleen will permit a more or less permanent relief from the symptoms of anemia, and by removing some of the burden from the portal circulation the tendency to ascites will be diminished He may enjoy several years of comparatively good health Undoubtedly he would have come to a fatal termination early if splenectomy had not been done

It is said that following splenectomy the prognosis in Banti's disease is better than in cirrhosis of the liver This is true only when the spleen has been removed before any important amount of cirrhosis in the liver has developed

A STUDENT Would you not, then, recommend splenectomy

in alcoholic cirrhosis of the liver and in syphilitic cirrhosis of the spleen?

DR BUCKMAN Yes, in general, and for the same reasons for which splenectomy was urged in this case

A STUDENT What is the significance of the cholesterol determination?

DR BUCKMAN In cases of hemolytic jaundice the cholesterol content of the whole blood is low, usually less than 100 mgm per 100 c c In cases of jaundice due to obstruction, as in this case, it is usually very high

A STUDENT What importance is to be attached to the digestion of the clot on incubation, fibrinolysis?

DR BUCKMAN Goodpasture has shown that in many cases of cirrhosis of the liver a fibrinolytic ferment is liberated In such cases, if the blood-clot be incubated at body temperature for several hours, the clot becomes digested and assumes a moth-eaten appearance When the test is positive it signifies liver damage, usually cirrhosis Are there any other questions?

A STUDENT I should like to know why an injection of sodium citrate was given to this patient

DR BUCKMAN You will remember that the coagulation time and the bleeding time were both prolonged Either the coagulation time or the bleeding time, or both, are frequently prolonged in cases showing jaundice and in which liver injury has occurred, and sometimes in cases in which no liver injury is manifest Why this should be the case is not known Possibly some anticoagulant, such as heparin, is set free

Now it has been shown recently by Newhof and Hirshfield that sodium citrate, given intramuscularly, causes a very prompt reduction in the coagulation time of the blood The effect lasts only a few hours, but is very marked It is supposed that sodium citrate causes destruction of blood-platelets, thereby liberating enough thromboplastic substance to permit rapid coagulation of the blood We do not know, of course, the mechanism of the action of sodium citrate All that we know is that it causes a reduction of the coagulation time, and at the same time a diminution in the number of blood-platelets It

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seems to work best in cases showing jaundice, and that is an important advance, because such cases are apt to show undue bleeding at operation and afterward Sodium citrate is said to be ineffective in thrombopenic purpura, perhaps because of the paucity of the platelets

A STUDENT What significance do you attribute to the presence of erythroblasts in the blood following splenectomy?

DR BUCKMAN The presence of erythroblasts, the increase in the number of platelets, and the increase in the number of myelogenous leukocytes from about 2800 to about 5600 are all indicative either of a lowering of the marrow threshold or a stimulation of the marrow. Practically it matters not which in this case This is the expected reaction from splenectomy in man The reaction occurs usually within two or three days, and is at its height, as a rule, by the tenth day Two weeks after splenectomy one expects to see a marked increase in the red cell count, as was the case here *Though this patient received by transfusion 300 c c of blood, it is hardly likely that this would cause a rise of 1,800,000 in the red cell count Ordinarily the introduction of 7 c c of blood per pound of body weight will cause a* rise of about a million in the red cell count On this basis his red cell count should have risen, on account of transfusion alone, only to the extent of about 900,000 per cubic millimeter of blood

In this case there was an increase of nearly 400,000 per cubic millimeter of blood in the platelet count Sometimes the thrombocytosis leads to the formation of thrombi, and these constitute one of the dangers of the operation of splenectomy

If there are no other questions, let us recapitulate the situation with respect to splenomegaly in children I have shown 4 cases, each representing a group, and into one of these four groups practically every case of enlarged spleen in a child can be placed These groups are the acute infectious group, the tumor group, the hemolytic jaundice group, and the cirrhosis group It is often difficult if not impossible to decide in the present state of our knowledge the exact diagnosis in a given case, but it is usually possible to tell whether the underlying condition is fundamentally an acute infection, a tumor, hypersplenism, or a

cirrhosis Removal of the spleen is, of course, contraindicated when the cause of the enlargement is an acute infection Except in the case of Gaucher's disease splenectomy should not be performed if the cause of the splenomegaly is a tumor in the sense here used On the other hand, benefit is to be expected from splenectomy in hemolytic jaundice and in cirrhosis of the spleen whatever the cause

It has been said that splenectomy should be done in every case in which an enlarged spleen persists unless an internist can show cause why the spleen should not be removed The burden of proof is put on the internist I should agree to this attitude, but it is important to remember that the internist can often show cause why the spleen should not be removed

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CLINIC OF DR LEWIS W HILL

CHILDREN'S HOSPITAL

TREATMENT OF MALNOURISHED CHILDREN IN PRIVATE PRACTICE

IN the last few years nation-wide attention has been called to the "undernourished child" Tens of thousands of school children have been weighed and measured, and nutrition classes have been formed in many cities Most of this has been done in schools by various public agencies and it is probably correct to state that, except among those pediatrists who are especially interested in the subject, the practitioner has paid but little attention to the problem of the undernourished child in his private practice Certain methods of treating malnutrition have been worked out for nutrition classes in schools by Dr W R P Emerson and others, and it is the purpose of this short "clinic" to urge that more attention be paid to undernourished children in the private clientele of each practitioner, and to show that the same methods used in classes can be applied to individual children in one's practice, with most excellent results

The type of child cared for is a child who is malnourished without any definite disease to account for it No child with such a condition as pyelitis tuberculosis, or chronic intestinal indigestion would be included The malnutrition is due more to faulty habits of eating and living than to actual disease What constitutes malnutrition? What is the distinction between bad and normal nutrition?

It has been held by many that if a child is 7 per cent or more below the average weight for his height he is suffering from malnutrition This is a rather arbitrary standard, and it is not desirable to follow it at all closely The general appearance of the child, his attitude, posture, muscular tone, and heredity must be also taken into account A child who is considerably

over the average height for its age is very likely to be under the average weight for its height In a recent examination of 106 children in a private school, 42 were found to be below the average weight for height, but 28 of these were considerably above the average height for age Of these 42, 18 were 7 per cent or more below weight for height, but only 5 could be definitely said to be suffering from malnutrition In another private school 78 children were examined, 38 were below average weight for height, 20 were 7 per cent or more below weight for height, but upon careful examination only 6 could be said to be really malnourished If one accepts 7 per cent below weight for height as a criterion of malnutrition, a large proportion of private school children who come from the best homes are malnourished If one takes into consideration the other factors which certainly should be considered, the proportion is not at all high It is a great mistake for a school physician to send word home to the parents that the child is undernourished simply because he is 7 per cent below weight for height The children who are below weight for height and *also below weight for age* are very likely to be suffering from malnutrition These two figures, taken in connection with the *general condition of the child*, serve as the best basis upon which to make a diagnosis of malnutrition

Treatment—Before treating any case definite disease of any sort must be first ruled out and a painstaking physical examination made Pyelitis, tuberculosis, intestinal parasites, intestinal indigestion, abscessed teeth, or diseased tonsils and adenoids may be found Chronically infected tonsils and adenoids are at the bottom of many cases of malnutrition, and these must be removed before the child can be expected to gain

There are two main factors in treatment plenty of rest, both physical and mental, and a high caloric, digestible diet If any individual rests a great deal and eats a digestible diet containing more calories than he really needs, he is bound to gain weight In a large proportion of cases, provided the right sort of home co-operation is obtained, good results may be obtained There are some children, however, who will never

be well nourished no matter how well they are cared for, how much they rest, or how much they eat In these cases it is probably a question of poor heredity more than anything else

In beginning treatment it is well to explain to the mother that if she is willing to take a considerable amount of trouble and report frequently to have the child weighed, good results can be obtained Occasionally a mother will not care to embark upon any definite régime that involves trouble, and about all that can be done for such cases is to give general directions for diet and hygiene, and let it go at that

In most cases, however, the mother is interested and is willing to go to any amount of trouble to have her child gain

For several years I have used the large charts provided by the Nutrition Clinics for Delicate Children, of 44 Dwight Street, Boston, and find that they are invaluable in enlisting the interest of the mother and child as well as furnishing a clear graphic record of the progress of the case A chart is reproduced on page 1580

The weight of the child is recorded on the bottom part of the chart and the correct weight for height on the upper part[1] The dotted line drawn from the normal weight for height represents the amount of weight a normal child of that age should gain week by week When the actual weight curve intersects the theoretic, the child is up to weight for height and is discharged At first weekly weighings are made, then biweekly The chart is made and pinned to the chart board at the first visit, and its significance and importance carefully explained to the child, the various dots and lines being made with different colored crayons A box of gold stars is produced and the child is told that he gets a gold star on his chart each time he gains weight It is of vital importance to enlist the interest of the child and, if a great deal is made of gold stars, fancy colored charts, etc , his interest is at once aroused

The child is also given a small blank book, and the mother is instructed to write down each day exactly what the child has

[1] The weight-height table used is the same one used by Nutrition Clinics for delicate children, and is based on the tables of Baldwin and Wood

eaten If he has eaten well, he gets a gold star on his book, and it is often surprising to see how much more interest some children will take in their meals if charted in this way

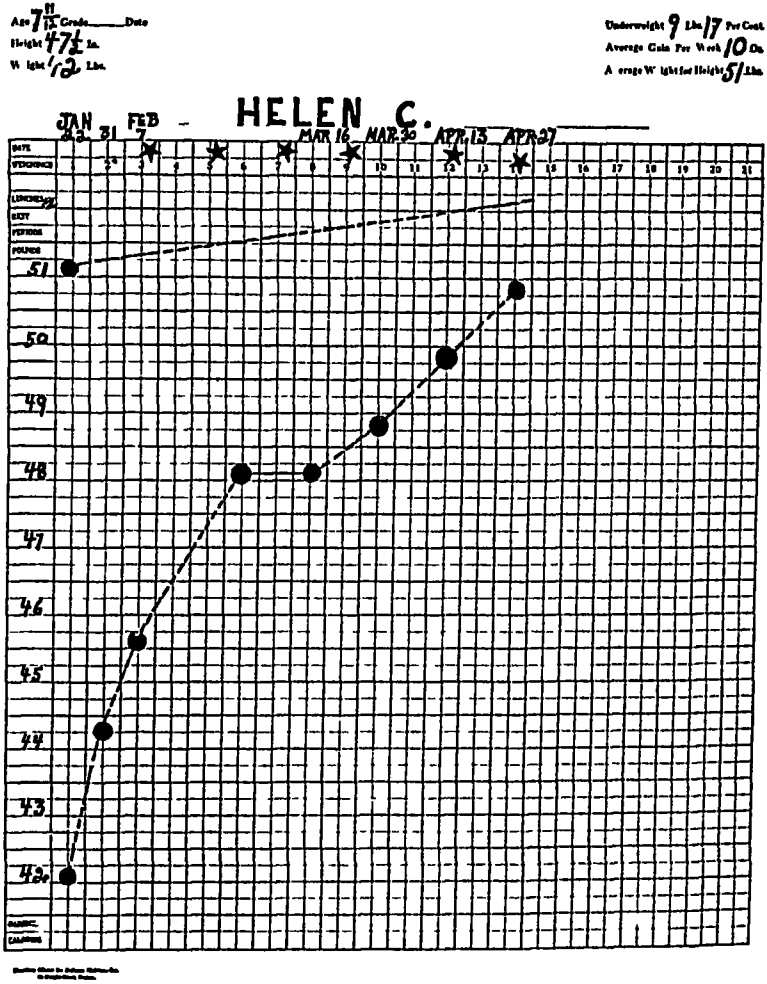

Fig 234

Rest —It is often hard to determine whether or not to take a child from school This has to be decided according to the circumstances, but, in general, the bad cases should be taken

from school, should stay in bed until 10 or 11 o'clock in the morning, sometimes for the whole half-day, and should have a rest of three-quarters of an hour after the noon meal No child who is under treatment is allowed to go to school two sessions, as this interferes with the rest period after the noonday meal, and also the exertion involved in four trips to and from school each day may use up a good deal of valuable energy The child must be kept free from nervous excitement, must not take too many outside lessons of one sort or another, must not go to parties, or away on visits It is surprising to see sometimes how a child will fail to gain some weeks when these weeks are broken A week end with the grandmother a movie, or a birthday party may be the cause of the failure to gain for the week

Under good conditions, the amount gained each week is often quite surprising Gains of 2 pounds per week are not infrequent The girl to whom the appended chart belonged gained an average of 10 ounces a week for fourteen weeks

Diet.—A high calorie diet is essential Some children with malnutrition have excellent appetites, some have not For the second group, having the mother write down each thing the child has eaten and putting a gold star on the book if the amount taken has been satisfactory, often works well

The following diet is the standard that is used for children from six to twelve years of age, and contains about 2200 calories It has been constructed with the purpose in view of giving as many calories as possible in an easily digestible form, and nothing is included that is not of high caloric value Thus, such vegetables as spinach, string beans, and celery are not allowed, as their caloric value is very low, and lima beans, beets, or peas are substituted It is often well to add a level tablespoonful of milk-sugar to each glass of milk taken This materially increases the caloric value of the diet without increasing its bulk No food is allowed which is not on the diet list, and the mealtimes are adhered to very rigidly It may often be necessary to modify the diet, as the children treated are of different ages and digestive capacities Some children may not be able to take as much fat as is contained in the diet If this is so, the

gravity cream is omitted and milk substituted There is nothing else in the diet that would be likely to cause trouble.

DIET LIST

		Calories	
Breakfast	One-half orange	50	
	One teaspoonful of sugar	25	
	Four tablespoonfuls of cereal	160	
	Three ounces of gravity cream	150	
	One egg	72	
	One pat of butter	100	
	Milk, 8 ounces	160	
	Total calories for breakfast		*717*
Lunch	Milk, 6 ounces	120	
	One Uneeda cracker	25	
	Total calories for lunch		*145*
Dinner	One chop or two slices of bacon	60	
	One potato	100	
	Two tablespoonfuls of peas, lima beans, carrots, beets, onions, or squash	50	
	One pat of butter	100	
	One half tablespoonful of jelly	50	
	Milk, 8 ounces	160	
	Two tablespoonfuls of bread pudding, baked custard, or apple tapioca	100	
	or		
	One tablespoonful of ice cream	100	
	Total calories for dinner		*720*
Lunch (3 P M)	Milk, 6 ounces	120	
	One cracker	25	
	Total calories for lunch		*145*
Supper	Four tablespoonfuls of cereal	160	
	Three ounces of gravity cream	150	
	or		
	Bread, two slices	150	
	Butter, one pat	100	
	or		
	Milk toast—one slice of bread	75	
	Three ounces of cream	150	
	One half pat of butter	50	
	Apple sauce or prunes or a dried fig or stewed apricots	75	
	Milk, 8 ounces	160	
	Total calories for supper		*485*
	Total calories for day		*2212*

OBSCURE CONTINUED FEVER DUE TO STARCH INDIGESTION IMPORTANCE OF IODOPHILIC BACTERIA IN THE STOOLS

I WISH to discuss today the differential diagnosis of continued obscure fever in a girl of seven years

A R was referred by her family doctor August 23 1923 The history was as follows

Family History —Only child No deaths or miscarriages No exposure to tuberculosis

Past History —Full term, normal delivery Normal at birth Birth weight 5¾ pounds Breast fed for three months, was then put on the bottle, and had a good deal of trouble with the feeding Since the age of two years she has had occasional periods when her bowel movements would be loose and undigested Whooping-cough last winter, and bronchitis for the last three winters Tonsils and adenoids removed two years ago

Present Illness —For about six weeks she has been running an afternoon temperature of 99 4° to 100° F Several times it has reached 102° F She gets tired very easily on slight exertion, and is always constipated Appetite poor No cough, no pain, or frequency of micturition No headache

Physical Examination —Looks rather poorly and pale Skin clear Tonsils out No tonsillar tissue remaining No tenderness over the sinuses No glandular enlargement Teeth excellent Heart negative Lungs negative No D'Espine's sign *Abdomen* slightly distended, and shows a few small superficial dilated veins No masses, spasm, tenderness, or evidence of free fluid Liver and spleen not felt

Weight, 47 pounds Average for age, 47 pounds Height, 47½ inches Average for age, 45 inches Average weight for height, 51 pounds

Blood examination shows a hemoglobin percentage of 90, and the smear shows no abnormality of either the red or white cells

We have here a girl who does not look or feel well, with an essentially negative physical examination, and who is running a slight but definite afternoon temperature

Diagnosis —There is a possibility that she may have one of three conditions Tuberculosis must, of course, always be considered when there is a continued slight temperature If she had tuberculosis it would probably be either of the tracheo bronchial or peritoneal lymph-nodes Pyelitis is another condition which very frequently gives rise to continued temperature without physical signs, and is very common in girls of this age Both of these conditions must be excluded

An intracutaneous von Pirquet test was done, and a roentgenogram of the chest was taken The von Pirquet test was negative, and the roentgenogram showed nothing abnormal This definitely rules out tuberculosis The urine was clear as water, and showed no albumin or sugar This rules out pyelitis

In view of the fact that this child has had a good deal of intestinal indigestion, it is not improbable that her trouble may be due to toxic absorption from the digestive tract Her bowel movement was very large, semiformed, acid in reaction, and showed under the microscope, when treated with Lugol's solution, a large amount of undigested starch and many iodophilic bacteria

In view of the history and stool findings a diagnosis of *chronic intestinal indigestion* due to starch was made

Discussion —Chronic intestinal indigestion due to starch is very common in younger children, and by no means rare in children as old as this The very severe forms, where there is extreme interference with nutrition, are not commonly seen at this age The symptoms are likely to be poor appetite, loss of vitality, failure to gain weight, and abdominal distention A slight fever such as this girl has had is not infrequent The nature of the bowel movements is quite characteristic There may be atonic constipation, or there may be too frequent stools, up to four or five a day The stools are always rather large and mushy, smell often somewhat like a pigpen, or sour, or foul, and are obviously undigested The microscopic examination

is of a good deal of value A small bit of stool is mixed with water on a slide, and a few drops of Lugol's solution added Undigested starch stains dark blue or black, sometimes in the form of round granules, sometimes in amorphous masses Potato starch is especially characteristic, and consists of many small granules enclosed in a thick cellulose sheath Also a good many iodophilic (black staining) micro-organisms are seen Some of these occur in chains, some in groups of one or two, and some in the form of thick rods or ovoids Inasmuch as they show well even under the low power of the microscope, they must be relatively large in comparison with the ordinary bacteria of the feces Some of them are probably yeasts and molds, some bacteria At any rate, their presence is of a good deal of significance, and they are always found in large numbers when there is starch indigestion If all starch is removed from the diet, they rapidly disappear and it is never wise to increase the starch in the diet of one of these cases as long as there is any considerable number of these iodophilic bacteria present

The presence of these organisms is always an indication of disturbed carbohydrate digestion, usually starch, and they are of considerable importance as a guide in regulating the diet, but I have never seen mention made of them in the literature except in a monograph by Paul Selter, published in Solingen in 1907, and translated by Herbert Rich, of Detroit Selter says "There is one kind of bacterium, however, which we can with certainty connect with a form of bowel disease It has been frequently observed that children fed richly on carbohydrate foods often have bacteria (in the stools) staining blue with iodin I have seen these iodin-staining bacteria in all forms, long, thin rods often piled up on one another—small, short, thick bacteria, and large yeast-like forms—others small ovals in bunches or chains like cocci, spindle forms, bullet-shaped, etc All these occur in pathologic stools, in any quantity, an occasional example being seen in an apparently normal stool The practical point is that these iodin-staining bacteria in large numbers are always connected with a carbohydrate disturbance, and this is a direct therapeutic indication"

Treatment—The treatment of such a case as this is almost entirely dietetic, and consists in greatly reducing the starch in the diet, or in the severe cases omitting it entirely Protein food in large amounts is substituted for the starchy food which has been withdrawn Often there is an intolerance for sugar as well as for starch, and in these cases it is not possible to use sugar in the diet Where there is no intolerance for sugar, milk-sugar, dextrimaltose, or Karo corn syrup may be added to the milk often in large amounts, and the caloric content of the diet thus greatly increased

The diet prescribed for this girl was as follows

Breakfast Half a banana or orange, 2 slices of bacon or a chop, 1 or 2 eggs, diaprotein biscuits, milk

Dinner Meat, 2 tablespoonfuls of spinach, celery, or string beans, 1 tablespoonful of rice, diaprotein biscuit, milk For dessert ice-cream, gelatin dishes, custard, or junket

Supper Milk, meat or eggs, or cottage cheese, diaprotein biscuits, 2 tablespoonfuls of applesauce or stewed pears

September 24, 1923 Weight 48 pounds, gain of 1 pound in a month Stool shows only a very little undigested starch, but still a good many iodophilic bacteria

Feels much better Treatment same

January 8, 1924 Weight 52¼ pounds Stool still shows iodophilic bacteria, but no starch

Treatment same, except omit rice, on account of the continued presence of iodophilic bacteria

February 26, 1924 Weight 53½ pounds, in excellent condition Stool shows no starch, and only a few iodophilic bacteria

April 9, 1924 Weight 54½ pounds Stool shows no starch and no iodophilic bacteria

October 21, 1924 Weight 57¼ pounds Stool shows no starch and no iodophilic bacteria

Treatment Same diet with the addition of two tablespoonfuls of cereal, or its equivalent in macaroni, rice, or bread

This child has been on a very careful diet, with practically no starch for almost a year now, and has gained 10 pounds

during that time The average gain in weight for a well child of this age in a year is 6 pounds The patient has, therefore, gained at a rate nearly double that of a well child

The High-protein, Starch-free Diet—In severe cases in younger children it is often necessary to remove all starchy foods, vegetables, and fruits from the diet Indeed, it is best to start all severe cases at once on such a diet It is not easy to plan an adequate diet for a small child when all the starch is removed, and for that reason such a diet is discussed below in detail Meat and milk form the cornerstones of the diet, and other foods used are eggs, cottage cheese, diaprotein biscuits and Karo corn syrup In some cases it may be necessary to use fat-free milk, in others whole milk may be given Whereas it is usually not desirable to allow a normal child to take over a quart of milk a day, many of these children can take with advantage as much as 48 ounces If the sugar tolerance is good, as it is in many cases, Karo corn syrup or dextrimaltose may be added to the milk, and furnishes a good many extra calories This should always be done if possible, and sometimes it is possible to get in 300 or 400 extra calories in the form of Karo Most writers in discussing the dietetic treatment of this condition, celiac disease, as it is often called, say that there is a *carbohydrate* intolerance, and recommend keeping the carbohydrate in the diet very low They do not distinguish between sugar and starch, *whereas it is a fact that many cases of starch intolerance have a very good tolerance for the more quickly absorbable carbohydrate sugar, especially when given in the form of corn syrup, and can take it with a great deal of advantage*

As much meat should be given to these children as they will take, and is almost always well tolerated A two-year-old child will often take 2 or 3 tablespoonfuls of chopped meat three times a day Meat is commonly supposed to be rather indigestible for small children, as a matter of fact, it is not, and especially in starch intolerance it is almost always handled well

The other articles of food that are used in the high protein starch-free diets are eggs, cottage cheese, and diaprotein biscuit One or two eggs a day may be given, either the whole egg or the

yolk alone If the yolk alone is used, a good way to give it is to boil the egg for fifteen or twenty minutes until it is hard, and then to grate the yolk and serve it moistened with a little milk

Cottage cheese may be made either from whole or fat-free milk Two teaspoonfuls of essence of pepsin are added to 1 quart of lukewarm milk This is allowed to "set" in a bowl until the curd has formed, then the curd is broken with a knife or fork, and whey strained off through cheesecloth, and a pinch of salt added to the curd One quart of skimmed milk makes about 6 rounded tablespoonfuls of cottage cheese

Diaprotein muffins are made from Diaprotein Flour, a starch-free, casein flour, prepared by the John Norton Company, of Columbus, Ohio

Fifteen level tablespoonfuls of the flour (1 ounce by weight) is mixed with one egg, 2 level tablespoonfuls of bacon fat or butter and 3 tablespoonfuls of water, and cooked in a biscuit tin in a *slow oven* This recipe makes six to eight muffins, which somewhat resemble small "popovers," and are not at all unpalatable Most children take them very well If the oven is too hot the muffins are likely to taste bitter, due to charring of the casein

The food value of these articles of diet is as follows

Milk

	Fat	Sugar	Protein	Calories
8 oz of fat-free milk	= 0 gram	11 grams	9 grams	80
8 oz of skimmed milk	= 2 grams	11 "	9 "	100
8 oz of whole milk	= 9 "	11 "	8 "	168

Chopped Chicken

	Fat	Protein	Calories
1 rounded tablespoonful	= 60 gram	5 grams	25
1 level tablespoonful	= 40 "	3 "	17

Cottage Cheese

Cheese from 1 quart of skimmed milk contains 30 grams of protein, and 120 calories 1 quart makes about 6 rounded tablespoonfuls of cheese

Diaprotein Muffins

Recipe 15 level tablespoonfuls diaprotein flour (10 ounces by weight)
1 egg
2 level tablespoonfuls of bacon fat
3 tablespoonfuls of water

This recipe makes 6 to 8 muffins, containing 460 calories 1 muffin contains 65 calories if 7 muffins are made

Eggs

	Fat.	Protein	Calories
Whole	5 grams	7 grams	72
Yolk	5 "	4 "	60
White	0 gram	3 "	12

Corn Syrup

1 ounce by volume contains 33 grams carbohydrate and equals 136 calories

1 teaspoonful equals $\frac{1}{2}$ ounce and contains 5 grams carbohydrate and 22 calories

IRON IN THE INFANT'S DIET

IRON is an important constituent of the infant's diet, as it is necessary for hemoglobin manufacture, and if an insufficient amount is given in the diet, the synthesis of hemoglobin is interfered with and the infant becomes anemic Human milk contains 0 55 mgm of iron per liter (expressed as Fe), a very small amount, it is true, but sufficient for the infant until the time of weaning Cow's milk contains only 0 17 mgm of iron per liter, and if the milk is diluted, as it usually is for purposes of infant feeding, this already minute amount is still further reduced So in the artificial feeding of infants the amount of iron in the diet is a question of considerable practical importance

Even with the extremely small amount of iron present in cow's milk, an artificially fed baby is not likely to become anemic on an exclusive milk diet up to the ninth or tenth month, as it has been shown (Bunge) that the young of all mammals are born with a reserve supply of iron in the liver to compensate for the small amount present in milk and to suffice for the iron needs until the infant can begin to take extra iron-containing food It has been shown that those mammals who naturally suckle the longest time have the largest reserve iron deposit

The iron in the fetal liver is mostly deposited during the last two months of pregnancy, so that one might expect that premature infants would have a tendency to become anemic at an early date, as they have an insufficient amount of reserve iron in the liver Such is the case, and it has been found by several observers that most premature infants begin to show an anemia at the third or fourth month Twins may also show this early anemia If the mother is anemic herself, or if she has eaten little iron-containing food during the last months of pregnancy, her offspring is born with an insufficient iron deposit, and is very likely to become anemic on the iron-poor diet whether it be breast milk or cow's milk

The natural inference to be drawn from these facts is that it is desirable to supply to normal full-term artificially fed infants during the last half of the first year, in addition to their milk, other foods which are rich in iron Premature infants, twins, and infants born of debilitated or anemic mothers should receive extra iron before this

Indeed, one of the chief purposes of giving a mixed diet to infants after the seventh or eighth month is to furnish iron, and at the present time it is almost universally the custom to do so Some of the foods which are given at this time, however, are not as suitable as others, and with this in view I have calculated the figures in the table below showing the amount of iron in ordinary measures of various foods It is not possible to determine directly the iron needs of infants, but by knowing the amount of blood added to the organism, as it grows from day to day, the iron content of the blood and the amount lost by blood destruction, it is possible to arrive at a rough estimate If one makes these calculations it is found that an infant of one year needs between 1 5 and 2 milligrams of iron in its diet each day in order to cover its iron needs [1] For a number of reasons egg yolk is the best food to use in order to supply iron It contains a relatively large amount of iron, it is almost always easily digested, and it is antirachitic It seems to be tolerated very well even by young infants, and may be given raw, shaken up with the milk, or hard boiled and grated, to older children

Fe Contents of Foods

	Milligram
Human milk, 1 liter	0 55
Cow's milk, 1 liter	0 17
Egg yolk, 1	1 4
Spinach, 1 level tablespoonful	0 59
Beef juice, 1 ounce	0 20
Prune sauce, 1 level tablespoonful	0 70
Oatmeal, 1 level tablespoonful	0 10
Rice, 1 level tablespoonful	0 05

[1] See Hill, L W, Boston Med and Surg Jour, vol 191, No 8, August 21, 1924

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ANGINA PECTORIS

Frequency of Signs and Symptoms Referable to the Gastrointestinal Tract Physical Findings as an Aid in Diagnosis and the Value of Absolute Rest in the Treatment of Some Patients

A CENTURY has passed since Jenner and Heberden noted the relationship of angina pectoris to lesions of the coronary arteries The progress made however in the study of this condition during these hundred years has not been gratifying Even now a controversy is being waged by clinicians over the cause and origin of the pain and the diagnosis of the disease is at times difficult and uncertain There is much indeed, that remains to be learned about angina pectoris Our knowledge of the normal capillary circulation of the heart for example, is almost *nil* while the pathologic physiology of the coronary circulation remains an unexplored field

This however, is not the time to discuss theories and possible explanations of the various points in the syndrome—matters well covered in the text-books—but it is perhaps a proper time and place to review briefly the condition itself in order to emphasize certain features that have been noted only to be slighted, and that have been refused their just places in the list of important signs and symptoms of angina pectoris Hence no effort will be made to discuss the whole subject, but attention will be confined to a few points

If one, in studying patients or the records of patients takes the trouble to make a chart of his findings, he is soon impressed by the frequency of some symptoms and the absence of others

It was rather surprising, for instance, in studying cases with coronary occlusion, to find in many instances that the thrombosis of the artery made the patient aware for the first time of severe heart disease Previous heart failure was rarely met with in such patients, although advanced arteriosclerosis was, as a rule, present

In angina pectoris arteriosclerosis is again, in most instances, the underlying process, and if one reviews a large number of cases with the primary diagnosis of angina pectoris, instances of heart failure will be uncommon This does not mean that these patients do not go to the stage of failure—they do—but it does mean most probably that the presence of pain has been a warning so effective that it has been generally heeded And when one sees the hearts of such patients at necropsy he is amazed at the fact that they performed as well as they did, for often the sclerosis of the coronary vessels has reached a stage where a pin can scarcely be inserted into their lumina The blood-supply to such hearts is certainly markedly decreased

The past history of a man with angina may be confusing or it may even be misleading unless one is familiar with the occurrence of symptoms pointing to other systems The frequency of gastro-intestinal disturbances, for instance, is striking, and at times they have been so misleading that exploratory laparotomies have been performed In a recent review of the records of 40 patients with angina pectoris it was found that 30 gave stories of trouble referred to the gastro-intestinal tract—"gas," "sour stomach," "indigestion," "nausea," and "nausea and vomiting" Many of the patients had taken soda, while others had been on special diets for relief, and in not a few instances physicians had made diagnoses of stomach lesions Rather significant is the fact that of those upon whom *x*-ray studies had been made, none showed lesions of the gastro-intestinal tract The importance of so frequent occurrence of gastric disturbance in these patients should not be overestimated but when a diagnosis is in doubt any additional evidence is helpful, and it may, therefore, serve as one more link in the chain

The origin of the gastric disturbance is undetermined Certainly it is not to be found in the common causes, such as ulcer or neoplasm, for in a number of patients who died following thrombosis of a coronary artery, a long history of epigastric pain, "indigestion," and other gastric symptoms was obtained Some of these patients had had angina pectoris for years but in no instance were gastric lesions other than arteriosclerosis discovered at necropsy It is possible that sclerosis of the vessels of the walls of the stomach and intestines might account for the symptoms, or it is not unreasonable to explain all the gastric disturbances as a reflex condition resulting from the changes in the coronary arteries Some support is given this idea by the fact that occlusion of a coronary artery very frequently produces an exaggeration of all the symptoms At best, the explanation is uncertain and deserves further study Despite the fact that we know so little of the cause of these disturbances, it nevertheless remains true that pain in the epigastrium, "indigestion," and numerous other gastric signs and symptoms are common, and the finding of these in people over forty years of age should direct attention to the heart and blood-vessels This does not, of course, mean that all elderly patients with such a history have angina pectoris The objection may be raised that 40 cases is too small a series from which to draw conclusions, and such a criticism is justifiable, but conclusions are not being drawn from 40 cases only This particular series of consecutive cases with a diagnosis of angina pectoris has been used merely to illustrate the frequency of gastric symptoms in groups of angina patients Many writers have mentioned these symptoms before, but without due emphasis

Another complaint frequently made is that of dyspnea on exertion and usually on very slight exertion, such as walking fast or walking against the wind This symptom often precedes the onset of anginal attacks, and is readily understandable when one sees the amount of sclerosis in the coronary arteries Indeed, after seeing the extensive sclerosis which occurs, one is at a loss to explain why all patients with sclerosed coronary vessels

do not have dyspnea or even heart failure, unless it be true that pain or dyspnea—in many instances paroxysmal—serves as an effective warning to limit further activity All patients with angina pectoris do not necessarily have coronary sclerosis Osler has reported deaths from anginal attacks in young people, in whose hearts no pathology was discovered

The pain—its distribution, character, and origin—has been the favorite point of discussion of all who have talked or written of angina, and many opinions on its various characteristics can be found in the literature It may not be amiss to point in passing to the fact that anginal pain is frequently located in the epigastrium—a point of some interest in view of the frequency of gastric symptoms before the actual anginal attacks begin A patient seen occasionally by the writer during the past five years illustrates the importance of giving due consideration to these digestive disorders in elderly people This patient was a woman seventy years of age, who for fifteen years had suffered from "indigestion," excessive "gas on stomach," and at times distress after meals During the past ten years the attacks had increased in frequency She described one as follows "The first thing I notice is a feeling of fulness in the 'pit of my stomach,' which increases so rapidly that I have to loosen my clothes in order to get my breath " On being questioned she stated that she never had pain either in the epigastrium or in the chest, but the fulness seemed to be due to gas in the stomach, was always accompanied by shortness of breath, and at times by nausea and vomiting Only during the last two years had these attacks come as often as once a week, and then they usually came from one to three hours after eating On several occasions an attack came immediately after a meal Finally, following a light meal, she noted a sudden distressing fulness in the epigastrium—not painful—but the distention was greater and she had to undress to relieve the "full feeling " A few minutes later she had marked dyspnea and began to vomit Her heart sounds, which had been very faint during previous attacks, could scarcely be heard in this one Her heart was slightly enlarged to percussion and the bases of both lungs were

filled with crackling râles Her skin was ashy pale, cold, and moist She died suddenly two hours after the attack began—the characteristic death of coronary occlusion Such a case presents vividly the relationship of gastro-intestinal disturbances to coronary disease, and no further comment upon it is necessary

Too little attention has been given to the value of physical findings in angina pectoris It is true that there exists no one sign characteristic of the condition, but there are one or two signs which may be of real value in the diagnosis The intensity of the heart sounds ought to be noted Of the 40 cases mentioned, only 12 were found to have heart sounds of normal intensity In all the others the sounds were described as "weak," "faint," "very distant," "barely audible" and "of tic-tac quality" These findings in routine physical examinations and in such astonishingly high percentage should give one pause and cause him to weigh, very carefully, the meaning of faint heart sounds This point has not received its just emphasis Few other cardiac conditions produce heart sounds of weak intensity, and when such conditions are present they are not difficult to recognize A thick chest wall or emphysema is apt to obscure heart sounds, but in very few instances of actual heart disease are the sounds "barely audible"

Other physical findings are less constant Cardiac hypertrophy may be found at times, although many patients whose anginal attacks are of years' duration may have hearts of normal size as shown by the 7-foot *x*-ray plate Signs of heart failure, particularly early ones, are sometimes present The appearance of fine crackling râles at the bases of the lungs is one of the earliest indications of failure, and this sign may be present for a long time before others appear Many patients with angina die suddenly as a result of coronary occlusion, but some go on to gradual heart failure—due most probably to a failing blood-supply to the heart muscle

It is surprising, when one consults the records of hospitals, to find so very few hospital deaths due to angina pectoris It raises the question as to how these patients die The answer,

in part, is to be found in the newspapers where one reads almost daily of sudden deaths It is highly probable that many of these people get a final occlusion of a coronary artery and drop dead, either from rupture of the heart or from ventricular fibrillation Others, of course, die of a gradual heart failure, and patients of this type are seen in hospitals and private practice For additional diagnostic evidence one may look to the electrocardiogram and may now and again obtain assistance from this source The notching of the QRS complex is, of course, well known and occurs frequently, though by no means constantly, for in patients with angina of long standing normal curves may be found The change in the QRS may vary from a slight notching to a marked spreading of the complex Left ventricular preponderance is common Rarely curves with low amplitude are seen, but this finding—a very frequent and significant one in cardiac infarction—is unusual in angina, though when present is one more bit of confirmatory evidence

Observations made at varying times on 35 patients indicate that the leukocyte count in angina attacks is normal The counts were never above 12,000 cells per cubic millimeter This fact, though seemingly unimportant, furnishes a good differential point between a simple anginal attack and the more serious attack resulting from thrombosis of a branch of a coronary artery The latter is almost invariably accompanied by a leukocytosis

Confusion of a simple anginal attack with occlusion of a coronary artery is not infrequent, and is due chiefly to failure to recognize the occlusion of the artery and the significance of its accompanying signs and symptoms The onset of the attack in both instances is sudden, and very often the location and radiation of the pain is the same, but the severity is much greater with the occlusion of the artery And while the pain may last minutes or longer in angina, it is generally relieved by nitrites In a patient with thrombosis, on the other hand, it lasts hours or days, and in many instances neither nitrites nor morphin give relief Early signs of cardiac failure accompany the

infarction—râles in the lungs, tenderness and swelling of the liver, and marked dyspnea and exhaustion on effort Finally, the presence of a leukocytosis and often of a fever makes it possible to differentiate an occluded artery from a simple anginal attack

The treatment of so common a condition as angina pectoris is not simple, at times it may necessitate a radical change in occupation and mode of life This is particularly true in instances where patients do strenuous manual labor One principle of treatment merits greater emphasis than it receives In many patients with angina fatigue and exhaustion play an important rôle, such patients are unable to respond to effort without pain or dyspnea, and the anginal attacks come at frequent intervals In these cases absolute rest in bed is indicated Mackenzie has advocated this repeatedly but one sees in hospitals and in private practice patients with angina of years' duration and in whom exhaustion is a prominent feature, but they have rarely, if ever, been treated by rest in bed

During the past year a man fifty-five years old, a foundry worker, has been followed closely in the Boston City Hospital In 1912 this man began to have anginal attacks and shortness of breath, and as a result was given "an easier job" Despite this, his attacks continued and he began to show signs of cardiac failure He then entered the hospital, and after a short rest was able to return to work and remained free from anginal attacks for several months Six months ago he began to have several attacks daily and a constant "constriction" in his chest He was placed at absolute rest, and after a month was able to return to his work and to continue working for three months without an attack Previous to this hospital stay in bed he had digitalis and nitrites and had "rested" at home, but without effect upon the frequency of his anginal attacks A month ago he came in again, his attacks of pain having become more severe and more frequent He was given theobromin and digitalis, with a resulting improvement in his dyspnea, but the painful attacks continued He was then put at absolute rest and the attacks

ceased in one week This is not an isolated instance, for many patients respond in a similar manner Drug therapy will frequently fail to diminish the number of attacks unless combined with absolute rest This combination is recognized as most efficient in treating more advanced heart failure and is in general use It will be found equally efficacious in some patients with anginal attacks and early signs of heart failure Rest in bed, therefore—absolute rest in bed—deserves a more prominent place in the treatment of angina pectoris

The value of digitalis and nitrites is too well known for comment The value of theobromin, however, is not so generally understood, indeed, in some parts of this country it is not used at all Its use is, however, based upon sound pharmacology One of the striking effects of theobromin is dilatation of the coronary arteries Good results, may, therefore, be expected from its use in angina pectoris, and, as a matter of fact, are frequently obtained Theobromin will give relief at times when nitrites fail, and if given daily may reduce the number of anginal attacks appreciably [1]

Of much greater importance, however, than isolated anginal attacks is the whole problem of treatment For the individual attack it is generally accepted that drugs are indispensable and almost invariably give immediate relief, but depending upon drug therapy alone is as unwise as depending upon rest alone A rational combination of rest and medication is the most effective form of treatment which can be employed The value of absolute rest in the cases in which exhaustion plays a rôle and in instances of the very early signs of heart failure should be borne especially in mind The importance of these therapeutic procedures is great, and when they are employed together with a careful and wise regulation of the patient's life and activities good results may be expected

[1] The dosage of theobromin sodiosalicylate commonly employed is 5 to 15 grains three times a day It is well to mention, also, that some patients are more susceptible to the drug than others, severe headaches or nausea and vomiting may follow its prolonged use or large doses

CLINIC OF DR HENRY JACKSON, JR.

BOSTON CITY HOSPITAL

THREE CASES SIMULATING NEPHRITIS

THAT the finding of albumin and casts in the urine does not necessarily indicate nephritis is a commonplace The physiologic and pathologic conditions giving rise to these phenomena are many and varied In most cases the underlying factor is evident or will become so under clinical observation The cause of the albuminuria in decompensated heart disease, in acute fevers and exanthemata, in the albuminuria of adolescence, and in that associated with menstruation or profound anemia or following severe exercise is usually self-evident and transient If, however, no adequate explanation can be found for such a disturbance in a given individual, and if the various transitory causes have been ruled out, the clinician must think more or less seriously of nephritis, but he should beware lest the inertia often following the establishment of a supposedly definite diagnosis blind him to further developments in the case and prevent proper evaluation of the slight, though often crucial, changes in the signs or symptoms that are shown Latterly chemical analysis of the blood and renal function tests of various sorts have been introduced to help the clinician toward a better diagnosis, and thus toward a more rational and a more accurate prognosis These tests are, without question, of great service, but in the last analysis they would seem to be of more value in the prognosis and the intelligent pursuit of the treatment than in the differentiation of a "functional" renal disturbance from the true though slight, pathologic change The moment we have tests sufficiently sensitive to detect very slight changes in renal pathology, then immediately do these tests respond to

those functional changes in the kidney associated with or caused by extrarenal factors, and thus the very purpose of the test is defeated In many cases where help is most needed we must rely largely or solely on the pure clinical data Sir William Osler quotes Thomas Fuller as saying, "The reasons drawn from the urine are as brittle as the urinal" Laboratory tests, by the same token, are of value only when accurately done, intelligently interpreted, and cast aside (in most cases) when they do not concur with well-established clinical evidence

That there are many cases diagnosed and treated as nephritis in which renal pathology is of minor importance or actually lacking is certain It is a diagnosis which allows great latitude in prognosis We have seen on the Fourth Medical Service at the Boston City Hospital during recent months several cases which were, for a time at least, diagnosed as nephritis, by ourselves or by others, which turned out to be something else It may be worth while to record these here

Case I—Admitted to the hospital September 19, 1924 Age sixteen White Male

Family history unimportant

Past History—Measles and pertussis several years ago Tonsils removed three years ago There have been no cardio-respiratory symptoms except slight dyspnea on exertion for several years The school doctor told him he had a weak heart There have been no gastro-intestinal symptoms, nor has he had any genito-urinary trouble except as related below in the present illness There was no history of venereal disease Best weight 106 pounds one month ago He thinks he has lost 7 pounds since then

Present Illness—Five years ago after exposure the patient went to bed one evening with a slight chill During the early morning hours he was wakened by a dull ache in the right upper quadrant and the right flank He passed blood in his urine the next day, and he continued to do so for a month, at the end of which time he was admitted to one of the large hospitals of Boston Renal calculus and tuberculosis of the

kidney were both considered, but no laboratory evidence for either of these conditions was forthcoming, and he was discharged with a tentative diagnosis of nephritis and a diet low in protein and low in salt There was no edema at this time His urine contained, however, much albumin and many casts

Five years elapsed without any special symptoms and the patient continued in good health

Five days before entrance there was a recurrence of the pain in the flank The pain was severe and radiated to the bladder He suffered from moderate nausea On entrance we found a well-developed and poorly nourished boy The head, eyes, ears, nose, and throat were negative There was slight tenderness in the right upper quadrant The urine on entrance had a specific gravity of 1015, was acid in reaction, and contained a slight trace of albumin, a rare granular cast, and a few red cells The phthalein test was 60 per cent in two hours Kidney plates at this time were negative for stone Cystoscopy was done and an a-ray after injection of the ureters showed a kinked ureter with a marked prolapse of the right kidney The patient was discharged without operative interference and was instructed in building up his bodily strength and weight as the best means of supporting his kidney and preventing a recurrence of the symptoms

As we saw the case it was not difficult to diagnose That it had been misleading may be seen by the fact that nephritis was the diagnostic label made by a large and thoroughly competent clinic A young boy does not do well on a low protein, low salt diet Undernourishment was marked on entrance and was a factor, in all probability, in the recurrence of the symptoms He had been unusually well while at a boys' camp a previous summer, and it was after his return to his home and to less satisfactory living and eating conditions that his second attack came on The diagnosis of kidney disease, like that of heart disease, is easier to make than to undo, and if, in addition, a young growing boy lives for a long period of time on a too low protein diet some damage to his general health may be done That a reasonable amount of protein damages the kidney even

when diseased is as yet unproved In advanced cases the clinical condition can be improved by such a régime and the blood chemistry may be brought back to normal But a prolonged diet of this sort may be harmful, particularly in a growing boy Many obese cases with high blood-pressure and slight renal involvement improve greatly under a diet calculated to reduce the weight, and this diet is very often relatively if not absolutely high in protein In the absence of nitrogen retention or other signs of defective nitrogen elimination it is probably unwise to limit too closely the patient's nitrogen intake, particularly in the case of a growing individual

Case II —White male, aged fifteen Admitted December 27, 1923, with a complaint of anasarca and a diagnosis by his private physician of nephritis

Family history negative

Habits good He does not smoke or drink alcoholic drinks

Past History —Scarlet fever a year ago followed by a normal convalescence Since that time he has had slight polyuria and nocturia quite generally once or twice a night There have been no other genito-urinary symptoms, nor was there any evidence that the urine contained albumin during the past year

Present Illness —About three months ago the patient began to notice that his abdomen was swelling, and at the same time his family noticed that his face and eyes were puffy There was no nausea, headache, or failing vision He felt weak and below par generally He was treated by his local doctor with a low protein diet, and the edema and ascites disappeared At the end of two weeks, however, these signs began to reappear and he was admitted to the hospital with a diagnosis of nephritis

On entrance we found a poorly developed and poorly nourished boy, mentally clear, but obviously quite sick The face was pale without any noticeable yellow color, the eyes were sunken and bright The heart, which was not enlarged, showed a soft systolic whiff at the apex and along the left sternal border There was slight dulness at the bases of both lungs, and over these areas could be heard medium moist rales The abdomen

was much distended and a definite fluid wave could be made out The extremities and scrotum were edematous On entrance the urine which was very scant in amount, showed a trace of albumin, many red blood-cells and a few hyaline and granular casts He seldom passed over 600 c c in one day, and the general average was 350 c c These urinary findings continued throughout the stay on the medical wards There was a slight secondary anemia The blood urea nitrogen was 46 6 mgm per 100 c c of whole blood The plasma protein was 8 43 per cent Thus he had a very considerable nitrogen retention and a normal plasma protein A few days after his entrance an abdominal tap was done and 500 c c of a light yellow fluid with a specific gravity of 1014 was withdrawn A two hour test was done which was interpreted as showing fixation of gravity during the day and a relative nocturia He was, however able to concentrate urea given by mouth very well indeed, and he excreted more than the usual percentage in two hours In spite of his high blood urea nitrogen he was able to handle simple nitrogenous substances well A tentative diagnosis of nephritis was made and he was placed on a low protein, low salt diet He did not respond to this treatment and a slight grade of jaundice was observed in the scleræ In view of this additional symptom of jaundice and the apparent ability of the kidneys to excrete urea normally, the diagnosis was reconsidered There were a few prominent veins in the abdominal wall, indicating visceral venous obstruction, and a prompt direct van der Bergh bilirubin test on the serum and a slight though persistent jaundice A moderate temperature of 99° to 100° F indicated an infection and tuberculous peritonitis and cirrhosis of the liver were both considered as diagnostic possibilities The von Pirquet test was, however, negative An exploratory laparotomy showed a small, nodular liver, probably an infectious cirrhosis

The case illustrates the conflicting nature of some laboratory evidence The blood urea was double the normal value, yet he was able to concentrate urea by mouth very well The two-hour test indicated a moderate renal insufficiency Yet

we were correct in casting aside this somewhat conflicting evidence and being led by the clinical data alone

Case III—White male, aged forty-five Admitted to the hospital July 11, 1924 He had been in the hospital a year before with a diagnosis of aortic insufficiency and cardiac decompensation For a few months before this entry he had been troubled with increasing dyspnea, edema of the ankles, nocturia, frequency, and some degree of nausea He had noticed no headache, and had had no trouble with his vision Otherwise his past history was irrelevant He had had no important infections and there was no history of venereal disease He improved under digitalis and rest, and his vital capacity rose to a normal figure of 4000 He left the hospital with a well-compensated aortic lesion and a "moderate degree of renal damage" He was well, however, for two months only, and he then began to have edema of the ankles, nocturia, and frequency Though his appetite continued good and he was subject to no gastrointestinal symptoms, he lost 15 pounds in seven months On his second admission he was dyspneic and cyanotic His teeth were very poor indeed, many being merely rotten snags, and pyorrhea was very pronounced The lungs were negative save for the fact that both bases were dull and many moist râles could be heard over these areas The heart was enlarged 2 cm to the left of the midclavicular line and was found 3 cm to the right of the sternum The heart sounds were of fair quality There was a short diastolic murmur in the third left space At the apex a loud systolic murmur was found The pulse was Corrigan in type The abdomen was negative except for the fact that the liver could be palpated several inches below the costal border There was marked edema of the extremities extending to the scrotum and the lower back

Under digitalis and rest he rapidly improved The dyspnea and edema largely disappeared and he felt very much better The pulse ranged from 80 to 90 A phthalein test done at this time was only 15 per cent The urine, with a specific gravity of 1012, contained a large trace of albumin, many granular

casts, and from 5 to 10 red cells per high-power field The blood urea was 57 8 mgm per 100 c c The red cell count was 2,300,000 The white cell count, 19,000 The whole blood uric acid (by Folin's latest direct method) was 6 2 per 100 c c The carbon dioxid of the plasma was 24 9 volumes per cent The patient showed at this time little or no cardiac decompensation This had virtually disappeared under effective and rapid digitalization The urine, the blood chemistry, and the renal dye test all indicated a far more severe renal involvement than could be accounted for by cardiac signs A nitrogen retention both of uric acid and urea and a very definite acidosis usually bespeak renal pathology if other causes have been ruled out, as they seemed to have been in this case In view of these facts the patient was placed on a very low protein diet Under this régime he seemed to improve definitely The blood urea nitrogen dropped to 34 8 and the alkali reserve rose to 35 5 volumes per cent. His red cell count, however, remained low and there developed a slight temperature Red cells continued to be found in his urine and the amount of albumin did not appreciably diminish After another two weeks of this treatment the blood urea nitrogen had fallen to a normal figure of 20 7 and the alkali reserve had risen to a normal value of 51 9 The hematuria continued, however, and the patient seemed clinically worse rather than better In the meantime a thorough search had been made for the source of the temperature, and pus had been found in the right antrum and the right sinus These were drained, with the evacuation of large amounts of foul pus It was felt that the source of the infection had been found and a rapid improvement was looked for The anemia grew worse, however It was the general impression that we were dealing with a rapidly advancing nephritis A transfusion was given The phthalein dropped to a trace and the blood urea nitrogen rose again to 51 3 mgm per 100 c c A renal a-ray showed no evidence of stone There were no petechiæ, the spleen could not be felt, and there were no sweats The fever, in spite of the adequate drainage of the antrum, continued to run from 99° to 102° F

The patient gradually failed and died on September 15th

At autopsy the following were the main findings The abdomen contained 925 c c of clear yellow fluid The right pleura contained 900 c c of fluid, which was clear, the left pleura contained 275 c c of blood fluid The pericardium was obliterated by fibrous adhesions The myocardium was negative The endocardium was negative except for the aortic and mitral valves, which showed extensive old and fresh vegetations, firmly attached and but little ulcerated The coronary arteries were slightly sclerosed The aortic valve was incompetent The spleen weighed 265 grams and contained an old infarct 1 cm in diameter The liver showed passive congestion The kidneys weighed 350 grams and each had an old infarct in the upper pole Otherwise the renal parenchyma was entirely normal There was no nephritis The diagnoses made were as follows

Vegetative endocarditis
Old pleuritis and effusion
Fibrinous pericarditis
General arteriosclerosis
Passive congestion of the liver, spleen, and kidneys
Infarcts of the spleen and both kidneys

Here was a case of malignant endocarditis which had been diagnosed and treated as a case of nephritis The blood chemistry indicated a moderate degree of nitrogen retention and a considerable acidosis These findings improved materially on a low protein diet Yet in spite of the fall in blood urea and the rise in alkali reserve the patient was clinically worse It is under such circumstances that laboratory data, particularly chemical data, should be cast aside A blood-culture would have settled the question, yet there were no indications of malignant endocarditis except those that might just as reasonably be ascribed to an advancing nephritis, with an associated infection of the antrum That the case presented, in any event, a hopeless prognosis is of little moment A low protein diet is hardly one which would be chosen to combat a severe general infection

In a doubtful case one should scrutinize carefully all the

clinical data at hand before making a diagnosis of nephritis, and one should be constantly on the alert for the development of new symptoms or signs which might turn the attention to some other disease Laboratory data are good confirmatory evidence, but rarely good contradictory evidence If one follows chemical data alone one will frequently be led astray In many cases the disease mistaken for nephritis offers no better prognosis than does nephritis itself, and hence but little actual harm is done Harm may be done however, in young persons by putting them on too low a protein diet for too long a time, and we have had one case which had been treated outside as nephritis which proved to have myxedema, and with the exhibition of thyroid this patient, as might be expected, improved very markedly

CLINIC OF DR FRANKLIN W WHITE

BOSTON CITY HOSPITAL

THE REDUNDANT COLON

THIS is an interesting and important anomaly of the colon which is fairly common, and which has been somewhat neglected in the text-books It is not an easy subject to look up There are a few valuable papers, but our systems of medicine say little about it

Formerly the redundant colon used to be discovered only as an occasional surprise at a surgical operation for serious symptoms, but now since the Roentgen ray has been used freely, we are getting a large and increasing amount of information about it We used to get a wrong impression of the disease from early surgery, which only discovered the severest cases, often at an emergency operation We have now a far better idea of its frequency and importance and diagnosis from the routine barium Roentgen-ray examinations, which are so common

The redundant colon is one that is too long for its owner This is not a matter of absolute length, because Bryant[1] has shown that the variation in the length of the colon in adults is all the way from 3 feet, 4 inches up to 10 feet, 10 inches in his series of 160 cases, but it is a matter of being too long for the individual abdomen and somewhat loosely attached, so that the colon falls into loops and kinks The redundancy may be general, that is, the whole colon may fit the abdomen badly, every part of it may be a little too long and too loose, or it may be local, so that we have simply a very long sigmoid loop in an

[1] John Bryant, Observations on the Growth and Length of the Human Intestine, Amer Jour Med Sci, 1924, clxvii, 499

otherwise normal colon (Fig 236) or a double loop at the splenic or hepatic flexure (Fig 239), or a very long transverse colon (Fig 245) Nearly two-thirds of the important loops are found on the left side of the colon, in the sigmoid, descending colon, or splenic flexure This looping and kinking of the colon may interfere with its function, and give rise to mild, moderate, or even very severe symptoms, which lead to confusion with other kinds of abdominal disease We have had one or two patients

Fig 235 —Normal colon (enema)

who had had an operation for supposed appendicitis, one or two who were worrying about the possibility of cancer, and others in whom diverticulitis and gall-bladder disease had been considered, and several with intermittent tumors, which were obviously fecal tumors, which came and went as the colon was unloaded

While the cause is usually considered a congenital one,

there is a certain amount of evidence that it is acquired in some patients by overloading and stretching the transverse colon and sigmoid in chronic constipation, and as a result of long abuse of cathartics

The most common symptoms are constipation, which is found in about three-quarters of the cases also with almost equal frequency pain, distress or gas in the abdomen The pain or distress may be local or general and varies in intensity from vague general discomfort to violent colics Vomiting occurs in about one-third of the cases Acute obstruction of the colon may occur rarely Volvulus of the colon, which usually involves the sigmoid, is never found unless the colon is redundant

In addition, there are other vague symptoms, such as headaches, malaise, irritability, fatigue, etc , which may be due to partial intestinal obstruction and toxic absorption, or may be of purely nervous origin At least one-third, perhaps more, of the persons who have redundant colons have no definite symptoms at all

A redundant colon may, of course, be found with some other lesion, such as abdominal cancer, an appendix, goiter, etc , but is far more commonly found alone The symptoms are not always in proportion to the length of the loops, but correspond rather to the degree of disturbance of colon function, and the tone of the colon and abdominal wall, and the sensitiveness of the nervous system In general, the longer the loop and the poorer the muscular tone, the more likely we are to have trouble The symptoms, like those of diaphragmatic hernia, are easy to understand after the *x* ray pictures are taken and the diagnosis established, but the lesion is practically impossible to diagnose definitely without the Roentgen ray

We must remember that a loop is not a stricture, it merely has a tendency to obstruct if it is overfilled, or twisted, or kinked Therefore the symptoms may be present only at intervals when these conditions are present The condition may be well shown by the routine barium meal given by mouth, but is usually more striking after the barium enema Both methods

are desirable, the enema to fill the whole colon at once and emphasize the loops, and the barium meal to show the effect of the lesion on the emptying of the bowel

The diagnosis is easy in the well-marked cases, but it is not always easy to draw the line between normal variations in the colon and mild redundancy It is well to be conservative in diagnosis, and not include too many mild cases in this group We must not make too much of a sigmoid loop a few inches longer than the average, or a hepatic flexure, or a descending colon that is a little wavy There is considerable normal variation in the length of the colon, as shown by Bryant's figures already quoted My impression is that there are many moderate, mild, and some severe cases

Case I.—Mrs C H L is a housewife of forty-two, with 2 healthy children She has always been well and strong, but has had several brief attacks of severe epigastric pain in the last few years In the last six months there were three severe attacks of epigastric pain, with vomiting, she has had constant, mild distress in the navel region, with no relation to meals, also some soreness or "pulling" across the lower abdomen, and she cannot lie on the left side at times There is intermittent constipation with laxative and enema habit, much gas in bowels relieved by enema, and attacks of diarrhea lasting two or three days Diagnosis of cholecystitis, gastric ulcer, and appendicitis had been made She had been given an ulcer régime without relief, and an exploratory operation was advised She has a lax abdominal wall, and the stomach contents after a test-breakfast showed low secretion without mucus or blood Roentgen examination a month ago, during an acute attack, gave bizarre pictures of the stomach (Fig 236), which was high and inverted, with the convexity of the curvatures upward, and the first portion of the duodenum pointing down There was a 50 per cent six-hour residue in the stomach The hepatic flexure was *above* and to right of the stomach, both flexures and the whole colon were greatly distended with gas At twenty-four hours the whole colon was filled, and a large long

sigmoid loop reached up under the liver, almost to the height of the hepatic flexure

A Roentgen examination repeated at the time of the first visit showed a stomach normal in outline and position, freely mobile, and empty in five hours The hepatic flexure was at the iliac crest, the appendix was long, wavy, mobile, and not tender There was a large, long sigmoid loop filling the mid-abdomen and reaching up to the transverse colon (Fig 237)

Fig 236 —Case I High inverted stomach with convexity of flexures upward, and first portion of duodenum pointing down, due to pressure of distended sigmoid loop F, Fundus, P, pylorus

The colon was well filled throughout at the end of forty-eight hours

The long sigmoid loop, causing partial obstruction with delayed emptying of the whole gastro-intestinal tract, the gas-filled colon, which pushed up and inverted the stomach, the intermittent colics, the previous wrong diagnosis and advice to have an exploratory laparotomy, make a striking picture of a redundant colon of severe type The first radiologist missed

the significance of the long sigmoid loop and obstructive signs, and made a diagnosis of probable gall-bladder adhesions Note especially the difference in the whole abdomen during and between attacks The stomach at one time is inverted and deformed, out of position, and slow in emptying, and later entirely normal in every respect The hepatic flexure was very high and gas filled at one time, and later normal in appearance

Fig 237 —Case I Redundant colon with long sigmoid loop reaching up to transverse colon

and position There are few other conditions which can produce such sharp contrasts in the position and function of the stomach and bowels at different times

The course was satisfactory, no operation was advised, but instead rest, abdominal exercises, a supporting corset, mineral oil by mouth and by rectal injection, an occasional enema With the exception of two mild attacks four months later the patient has remained entirely well for six years

Case II—Mrs N C R is a housewife of fifty, of very nervous disposition, a poor sleeper, always tired, a great worrier, with frequent attacks of typical migraine for the last fifteen years She has persistent constipation with daily laxatives, and for thirty years intermittent indigestion, gas in bowels and much belching, distress and soreness in the abdomen, especially in the right upper quadrant Enemata were used frequently for relief Motoring "pulls on the right side" There was no vomiting except with migraine, no colics, and no jaundice She is very much worried about her health and the question of an operation, as a diagnosis of chronic appendicitis has been made

Physical examination shows a rather plump, flabby woman with dark circles about her eyes, and a red fissured tongue and very active reflexes She has a poor posture and relaxed, pendulous abdomen The stomach contents after a test-breakfast shows normal secretion without mucus or blood

Roentgen examination shows the stomach normal in position The antrum is somewhat narrow and elongated The pyloric region and first portion of the duodenum do not fill well even after prolonged observation The second portion of the duodenum runs rather far to the right, and curves downward at an angle The stomach tends to double on itself when the patient lies prone After six hours there was a trace of the barium meal in the stomach The appendix was normal in outline and position, and not tender The right side of the colon went up under the diaphragm *above* the liver (Fig 238) There was a large amount of gas in the hepatic flexure, 5 or 6 inches in diameter *above* the liver The outline of the right diaphragm was seen as a clear arch above the gas, which is much larger than an ordinary gas-bubble in the stomach At the end of twenty-four hours the colon was almost empty, and in practically normal position, with no gas in the hepatic flexure, and the liver fits closely under the diaphragm (The patient insisted on using a cathartic during this twenty-four hours for relief of distress, and had several loose stools) Gall-bladder plates showed nothing abnormal

The Roentgen examination was repeated in a month, and again after eight months, with exactly the same results, except that there was a delay of one or two days in emptying the right side of the colon when no cathartics were used

The diagnosis was made of a redundant and very loosely attached right half of the colon, which is very variable in position, with frequent pocketing of gas in the hepatic flexure under

Fig 238 —Case II Redundant colon with hepatic flexure greatly distended with gas *above liver* The arch of the right diaphragm (D) is just above the gas, L, upper liver border The contents of the colon are liquid and fermenting

the right diaphragm and above the liver The deformity of the pyloric region was considered due to the pulling and twisting of the omentum

An earnest effort was made to improve the patient's condition by mental hygiene, rest and sedatives, and to check fermentation and promote emptying of the bowel by a suitable diet, mineral oil, enemata and occasional mild laxatives, and

to strengthen the abdominal wall and improve muscular tone by exercises and supporting corsets We had only partial success, there were periods of improvement, with a strong tendency to relapse Several surgical consultations were held, but she decided that she did not suffer enough "to risk an exploration," and she was not urged The striking features of this case were the very unusual length and position of the hepatic flexure, with the pocketing of gas and feces *above* the liver, and the unsatisfactory results of treatment Marked neurasthenia and a redundant colon make a very unhappy combination

Case III—Mr H J is aged sixty-eight, with arteriosclerosis and hypertension, with previous dizziness, and a cerebral hemorrhage four months before, with a left hemiplegia from which

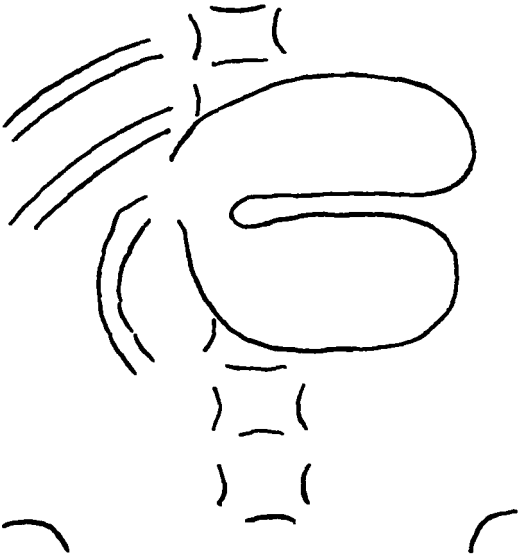

Fig 239—Case III Peculiar distorted stomach, due to pressure of great splenic flexure loop of redundant colon Stomach spherical, deep incisura, no clear pyloric outline

he gradually made a complete recovery Ten days ago he was seized with a sudden severe pain in the epigastrium after carry-

ing a hod of coal upstairs He vomited repeatedly, the vomitus was not characteristic, showed low, normal gastric secretion, and contained no blood The pain persisted in varying degree for nearly a week, working toward the left side, and especially the left upper quadrant He was in bed for a week, and required morphin twice The bowels are ordinarily regular, as a rule, but he was obstinately constipated during the attack, the abdomen felt blown up, and there was much gurgling of gas

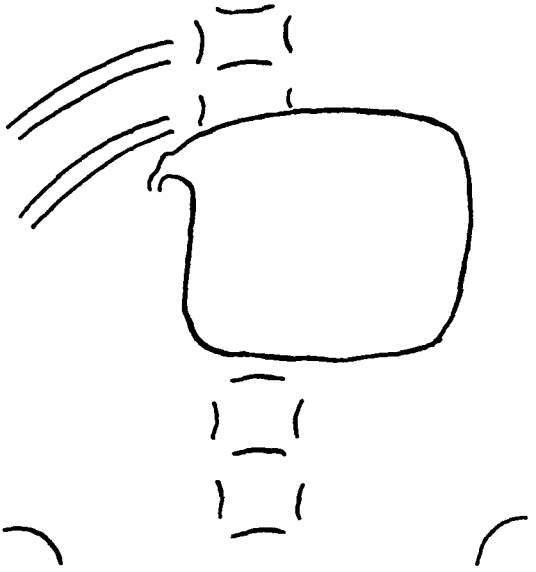

Fig 240—Case III Peculiar distorted stomach, due to pressure of splenic flexure, loop of redundant colon The duodenum apparently opening off the upper right-hand corner

Enemata, stupes, glycerin suppositories, and cathartics were used, and much gas was passed with relief There was no blood in the stool, either gross or occult, and no jaundice He had one similar attack eight months before, lasting four or five days

Physical examination showed arteriosclerosis, some emphysema, and an abdomen distended and tympanitic, especially in the epigastrium and left upper quadrant, with no definite masses or spasm He had a small epigastric hernia which was

not tender He was referred to the hospital with the diagnosis of probable malignant obstruction of the splenic flexure

Roentgen examination showed a very peculiar stomach (Fig 239), almost spherical in outline, with a deep, narrow incisura dividing the stomach into two equal parts, and no clear outline of the pylorus or first portion of the duodenum At six hours there was a 25 per cent residue in the stomach and at twenty-four hours there were traces of barium still in the

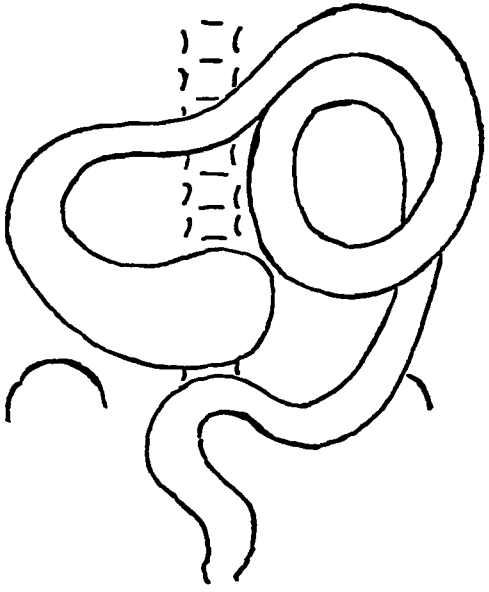

Fig 241 —Case III Redundant colon, with large circular loop at splenic flexure Cecum is freely mobile and occupies midabdomen (Case III Sketches were made at fluoroscopic examination, the plates were lost)

stomach and in the small intestine, and the colon was well filled as far as the splenic flexure, but not beyond The left diaphragm was a little higher than the right following the left hemiplegia The report of the roentgenologist was probable gastric cancer A second examination a few days later showed a stomach of entirely different shape (Fig 240), almost square, with no incisura, and the duodenum apparently opening off the upper right-hand corner A third examination of the stomach

at the end of a week when the attack had subsided showed it *entirely normal in position and outline and emptying within the normal time* A barium enema showed a loosely attached colon (Fig 241), with a redundant, circular loop of splenic flexure, large in caliber, and almost 8 inches in diameter, filling the whole left upper abdomen The cecum was freely mobile and occupied the middle of the abdomen

A diagnosis was made of a redundant colon with a large, splenic flexure loop, causing partial obstruction of the bowel, and marked deformity of the stomach by pressure and twisting

The patient steadily improved The bowels became regular and he left the hospital in three weeks He was given advice similar to Cases I and II regarding the care of the bowels, and there has been no recurrence of symptoms in the last year

The outstanding features of this case are the advanced age of the patient at the time of the first attack, the incorrect early diagnoses, the *very variable deformity of the stomach*, suggesting at first possible cancer, and later deformity from external sources, such as pulling or twisting, and later still becoming entirely normal, the large circular redundant loop of the splenic flexure, the lack of habitual constipation, and the non-recurrence of any important symptoms in the last year

We have seen a much larger number of cases of redundant colon of mild and moderate grade without severe obstructive attacks, but with various combinations of constipation, gas distress, discomfort or pain in the abdomen, and showing all kinds of loops and kinks involving the sigmoid, splenic, and hepatic flexures We shall only discuss 2 of them

Case IV.—Mrs L E is a widow with 5 children, living an active outdoor life on a large farm A hysterectomy was done six months ago for fibroids, and a left nephrectomy soon after for a damaged ureter Convalescence was rapid and complete, and she considered herself well until three weeks ago After walking up a hill and going up a steep flight of steps she had some pain and soreness, and a "drawing" feeling low in the right side of the abdomen, and felt a mass in the right side Her local physician

has felt a sausage-shaped mass in the right flank several times in the last three weeks, and sent her in for examination The bowels move daily without diarrhea or constipation She has a good appetite and there was no indigestion save vague gas in the bowels Senna has been given twice followed by four or five stools, without change in the mass There was much gas in the bowel, and the right side of the abdomen showed tympany

Fig 242 —Case IV Redundant colon with sigmoid loop (S) reaching up almost to splenic flexure

and slight fulness The whole colon was vaguely tender, but no mass was felt on repeated palpation before and after enemata A preliminary diagnosis was made of probable postoperative adhesions with partial obstruction of the bowel

Roentgen examination showed a very redundant loosely attached colon (Fig 242) with a long sigmoid loop, and much convoluted rectum There was great difficulty in giving the enema on account of gas in the bowel It took nearly 4 quarts

to give complete filling and there was a long delay at the junction of the sigmoid and descending colon and at both flexures, which were filled with gas, there were no adhesions

The interesting features of this case are the intermittent tumor, which must have been colon, distended with gas or feces, either the long sigmoid loop or the obstructed colon above it, and the reference of pain to the right side of the abdomen when the actual lesion was on the left An obstruction in the sigmoid region may throw back the fecal column into the blind end of the colon namely, the cecum, and the pain, distress, or dragging sensations be referred to the right side or right lower quadrant The usual treatment was given, a bulky, soft diet, lubrication from above and below with mineral oil, rest, and general sedatives There were only one or two slight recurrences in the following year, and the patient considered herself well at the end of that time No more masses were felt

Case V —Mrs E H is a flabby, rather fat married woman of forty-six, who leads an indolent life She has been constipated for years, and has used laxatives Her favorite is an ounce of Pluto water daily In the last two years she has had much gas in the stomach and bowel, and is an inveterate cribber There is some general tenderness and distention, and rumbling in the abdomen, which is relieved by rubbing and enemata She has abdominal massage twice a week Occasionally she has severe pain, which is variable in position, sometimes in the epigastrium, sometimes in the lower bowel It comes most often after meals, and is best relieved by an enema, there is much relief if the gas is passed freely, and distress if it is passed slowly She has worried about the possibility of cancer, and has been suspected of gall-stones A barium enema showed a very unusual picture of a colon which is loosely attached and redundant throughout (Fig 243), with a long sigmoid loop and long transverse colon, and a large loose cecum occupying the middle of the abdomen After barium by mouth the colon took two to four days to empty without laxatives

We have here all the ordinary symptoms of a redundant

colon—obstinate constipation gas distress, pain plus discomfort in the abdomen, cathartic habit, relief by enemata and abdominal massage, and a striking Roentgen picture This patient has been much improved by the usual treatment already outlined, but could not be kept entirely well

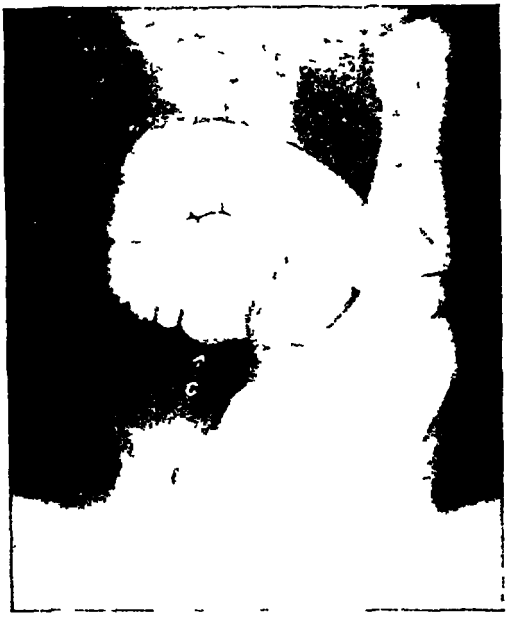

Fig 243 —Case V Redundant colon with long sigmoid loop, long transverse colon, and cecum (C) in midabdomen

Frequency —In looking over 1000 consecutive private gastrointestinal cases in whom routine histories, physical examinations, test-meals, and Roentgen examinations are recorded, we have found 43 cases with varying degrees of redundancy of the colon, 9 were severe, 34 were moderate or mild This 4 3 per cent probably falls short of the number actually present, as barium enemata which showed the condition best were given in less than one-fifth of the patients This percentage would be still further increased if mild and borderline cases were included It is not fair to include ptosis cases where the colon is

loosely attached, and where there is only a mild extra looping at the hepatic flexure or where the flexures double over in the erect position This was recorded 15 times in the 1000 cases

Kantor,[1] in a similar series of 668 cases, found 9 2 per cent of redundant colons The most accurate estimate of frequency will come from postmortem studies, since many patients with a redundant colon have few or no symptoms and do not consult a doctor, or do not have a sufficiently careful examination to dis-

Fig 244 —Redundant colon with very long sigmoid and descending colon loops, one of which passes in front of transverse colon

cover it Bryant's[2] postmortem figures give 15 per cent of elongated (redundant) colons in 160 cases

The *position* of the redundant folds or loop was on the left side in the majority of cases, namely, 24, with 16 in the sigmoid

[1] John L Kantor, A Clinical Study of Some Common Abnormalities of the Colon I The Redundant Colon, Amer Jour Roentg , 1924, xii, p 414

[2] John Bryant, loc cit

and 8 in the splenic flexure, this included most of the serious cases In 3 there was general redundancy of the whole colon, and in 16 it involved the hepatic flexure Here the folds were small and the symptoms mild, with a few exceptions, one of which was Case II, where the hepatic flexure passed up between the liver and diaphragm (Fig 238) On account of the loose attachment of the redundant colon the position and size of the

Fig 245 —Redundant colon with very long transverse colon

loop varied greatly at different times, this was particularly true of long sigmoids which at one time would coil up in the pelvis, at another time would reach over to the cecum and again would run up parallel with the splenic flexure We have shown in Cases I, II, and III what extraordinary and variable deformities of the stomach and duodenum can be produced by the pressure, twisting, and pulling of the great colon loops, filled with gas or feces (Figs 236 239, 240)

Contrary to our expectations, there were only 17 women to

26 men in the group that is, about 63 per cent were men, and only about one-third of the whole group were of the ptotic asthenic type The average or strong physique predominated One patient was a professional athlete, another a naval officer The redundant colon is by no means confined to weak people

Symptoms —*Constipation* was the commonest symptom, being found in 30 cases, or about 70 per cent It usually was of many years' duration, and the patients were laxative and

Fig 246 —Redundant colon with long sigmoid and loose splenic flexure (arrow) which has doubled over, and cecum which slides over into left pelvis

enema habitués This is easy to understand on account of the mechanical hindrance offered to the emptying of the bowel

Gas with abdominal distress was the next symptom, which was found in 27 cases, or about 63 per cent We have considered this also as a partial obstruction symptom It may also be due, as Kantor has pointed out, to poor absorption of intestinal gases by interference with the blood-supply to the colon, by twisting and kinking of the colon loops It was often general,

sometimes in the upper abdomen, sometimes in the lower It was associated often with cribbing and belching gas, and was naturally relieved by passing flatus or the use of enemata

Pain in the abdomen has been an important symptom, present in 27 cases, or 62 per cent This has varied in degree from mild grumbling to violent colics, and has led to many wrong diagnoses It has often been general, and sometimes variable in

Fig 247 —Redundant colon with enormous cecum (C) occupying the middle of abdomen

place, which is easily understood from the varying position of the colon loops, and varying degrees of pressure, twisting, and obstruction When local it has been twice as frequent on the left as on the right side As in Case IV, an obstruction in the sigmoid may throw back the fecal column into the cecum, and give pain in the right lower quadrant No case in this group has required operation for acute intestinal obstruction (volvulus), but one or two cases have come dangerously near it

Vomiting and *diarrhea* have also been occasional symptoms Vomiting occurred in 12, and diarrhea in 4 cases of the group These are not distinctive symptoms, but simply show the presence of abdominal disturbance and reversed or hurried peristalsis The vomitus has not been characteristic, and the diarrhea evidently due to colon irritation, or the unloading of a partly obstructed bowel Mucus was occasionally present in the feces, but no blood

Fig 248 —Redundant colon of long straight type Note extreme length of ascending colon (between arrows)

Intermittent tumors were a feature in 3 cases An example is seen in Case IV, obviously due to colon loops, or obstructed colon filled with feces or gas Serious tumors of the bowel were suspected until their nature was discovered

It is interesting to note how very closely this group of 43 cases compares in frequency, sex, relation to ptosis and asthenia, colon outline, and frequency of symptoms with the series of 62

cases recently reported by Kantor[1] We must be dealing with a definite entity with a quite constant incidence and clinical picture

Diagnosis.—In not one case in our group has a positive diagnosis been made till after the Roentgen examination. The symptoms are logical and easily understood when once the diagnosis is made, but are of a general character and not diagnostic

Fig 249.—Redundant colon with very large hepatic flexure (H) and long sigmoid loop (S) which lies in front of cecum.

alone There is a close similarity in this respect with the much rarer condition, diaphragmatic hernia of the stomach

The redundant colon is a definite entity which is fairly common, which is important to remember in constipation and in abdominal diagnosis when general abdominal symptoms are present or local painful attacks It is very important to avoid wrong diagnoses of other lesions which produce colics or ab-

[1] John L. Kantor, loc. cit.

dominal distress, or pain, such as disease of the gall-bladder, or appendix, or cancer, or diverticulitis of the colon, and thus avoid unnecessary exploratory operation and the removal of harmless organs In no other disease are such striking, peculiar, and variable deformities of the stomach seen except in diaphragmatic hernia

The Roentgen picture has already been sufficiently emphasized, the position, variability and extent of the loops of colon,

Fig 250—Redundant colon with large, high, hepatic flexure (H) and low splenic flexure (S), an unusual type

the hepatic flexure sliding up between the liver and diaphragm, the gas distention of flexures and loops, the delay in emptying the colon, and the occasional strange pictures of the stomach Both barium meal and enema have their place, the meal to show the effect of the lesion on the emptying of the bowel, and the enema to fill the whole colon at once and outline the loops If the enema is only occasionally used, some cases will be missed

Treatment—The bowel must be treated kindly and let alone as far as possible, the patient rarely sees this, and has usually "beaten them up" with a long course of laxatives and cathartics, which have only added to the irritation and spasm, and often made matters worse A bulky diet is essential, giving plenty of cooked fruit pulp and mashed vegetables, which are often better than coarser food, such as bran and raw vegetables, when there is much irritation of the bowel Instead of irritating cathartics we lubricate the bowel from above and below by mineral oil by mouth and 6-ounce oil injections at bedtime, which are retained, if possible, overnight Enemata we avoid if possible, and only occasionally use bland enemata of bicarbonate of soda, 2 teaspoons to the quart of warm water, which is far less disturbing than the usual suds enema Rest and tonic measures are needed for the tense, nervous cases, and occasionally sedatives and belladonna

The results of treatment have been very satisfactory in a large majority of the patients, especially those of mild and moderate grade, and even in some of the severe ones, such as Cases I and III A glance at some of the Roentgen pictures will show that we can never expect to make such colons anatomically normal, but we can often restore normal function and make the patient symptom free There is always an accidental feature in these patients Some of the worst cases with the largest and longest loops may go for long periods without chronic symptoms or an acute attack

No surgery, such as the fixation of the colon or resection of loops, has been attempted in this group, as it seemed likely to make matters worse It is possible that in a rare chronic case a resection of a long troublesome sigmoid loop might be profitably done A twist of the sigmoid (volvulus) with serious acute obstruction requires immediate surgery

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HOW MUCH DO WE KNOW ABOUT THE RELATIONSHIP BETWEEN URIC ACID AND GOUT?*

I. INTRODUCTION GARROD THE HIGH LEVEL OF CIRCULATING URIC ACID IN GOUT THE KIDNEY AND THE URIC ACID

THE clinical picture of gout will always remain intimately connected with the name of Sir Alfred Baring Garrod[1] His description of this disease as given in his famous treatise, published in 1860, left practically nothing to be added The subjective symptoms had already been described in an admirable way two centuries before Garrod by Sydenham, himself a sufferer from the disease Modern clinicians have merely kept the classical knowledge alive, transcribing it into present-day medical terms

As to the theory of gout, we find that already before Garrod a connection between gout and uric acid was fully recognized The presence of urates in tophi of patients suffering from attacks of gout, repeatedly proved in a satisfactory way, was a finding too significant to be overlooked or forgotten And it is more than possible that Garrod built his well-known gout theory

* Read, in abbreviated form, before the New York Academy of Medicine, January 20, 1925

more upon these observations than upon his own blood analyses —at least he had in the former a solid rock to build upon—while his estimations of the uric acid content of the blood have not stood the test of time

Just as the clinical description of gout has remained unchanged, so the problem of the underlying disorder has remained unsolved, notwithstanding numerous attempts to reveal its secret

When we* still consider an abnormal elevation of the uric acid level of the blood as a fact of primary importance in the interpretation of this strange disease, we seem to follow Garrod, only, modern methods have given us exact knowledge on a point where Garrod, in fact, operated with a guess—a guess which, however, turned out to be correct †

As is well known, Garrod interpreted this high blood uric acid as being due to a very specific kind of kidney insufficiency, an inability to properly excrete uric acid, while other products are eliminated in a normal way Without any essential changes this interpretation has survived up to the present day, Thannhauser being its most modern supporter

A more intimate study of the uric acid excretion, both in different animals and in normal and gouty individuals, has forced us to adopt a somewhat different view From our injection experiments with uric acid solutions it appears that the gouty kidney is fully able to excrete any excess of uric acid present in the body Yet the blood uric acid is constantly elevated We, therefore, deal with an unsensitiveness rather than with an insufficiency This may sound like a rather academic distinction A comparison of the conditions in different species will

* The following presentation is chiefly based upon a study of the uric acid problem by Folin, Derick, and myself (Jour Biol Chem, 1924, 60, 361–471) For the experimental evidence for the conclusions set forth on the following pages the reader is referred to this publication References not found at the end of the present paper are to be found in our joint publication

† Some readers will believe this to be an unjustified statement It might then be recalled that Garrod demonstrated increased amounts of uric acid in the blood in gout, but at the same time failed to find any uric acid in the blood from different birds, where the uric acid content is about the same as in the majority of gout cases

demonstrate what I mean In the goat and in the dog, for instance, the blood is practically free from uric acid (less than a mgm per 100 c c), and still uric acid is excreted in the urine The kidney in these animals possesses a high sensitiveness for circulating uric acid, and practically none is allowed to accumulate in the blood That this interpretation is correct and that elimination rather than destruction of uric acid here is the factor concerned is clearly demonstrated by the behavior of the Dalmatian dog This animal destroys, under ordinary conditions, no uric acid, or only minimal amounts of it But in spite of a uric acid output more than three times as large as the output of a normal man, calculated per kilogram body weight, the blood-plasma of this peculiar dog is just as low in uric acid as the plasma of any ordinary dog Versus this highly efficient kidney the *normal* human kidney shows a most surprising unsensitiveness just for the removal of the uric acid—5 5 mgm and even 6 mgm uric acid per 100 c c plasma being a normal finding in young, healthy individuals, living on an ordinary mixed diet

That this unsensitiveness of the normal human kidney is a specific phenomenon concerning the uric acid alone is indicated by the fact that no analogous difference has been demonstrated in the concentration of other waste products in the blood of man and of other mammals, when compared under similar dietetic conditions

We are now ready to return to the gout problem, and I hope we are also able to agree that instead of the hypothesis of Garrod, we are in possession of plain indisputable facts showing a definite unsensitiveness for uric acid on behalf of all human kidneys And we seem to be fully justified in interpreting the abnormally high level of circulating uric acid in gout as a *pathologic accentuation of this unsensitiveness*

One cannot help wondering whether in this behavior of the kidney toward the uric acid we have struck a really specific phenomenon, or whether it is only due to our inability that we have failed to demonstrate the same for other waste products as well There is some further experimental evidence, pointing, I believe, in the direction of the former assumption

When uric acid, *in the form of a lithium urate solution*, is injected intravenously into an animal under ether, and with the abdominal organs and the kidneys exposed to direct inspection, a most interesting observation can be made While the other organs show no gross changes, the kidneys during the course of the injection rapidly become swollen pale, with a shiny surface, and quite hard at palpation From the sectioned kidney a large amount of clear fluid runs off The chemical analysis shows a concentration of uric acid in such a swollen kidney (the loss of fluid having been prevented by freezing the organ before any further procedures) amounting to twenty times or more the concentration in the blood In sharp contrast to this we find all the other organs practically impermeable to uric acid, the muscles, only after prolonged exposure to high blood uric acid concentrations, coming up to about a tenth of the concentrations in the blood (in ducks after ligation of the ureters) Repeating the experiments with injections of urea and of creatinin, we again meet with results placing the uric acid in an exceptional position The urea and creatinin are not concentrated in the kidney tissue in the same way as the uric acid This extraordinary absorption of uric acid by the kidneys is not a harmless process In our animal experiments, undertaken with larger doses than our human experiments, albuminuria and general impairment of the kidney function followed, even complete anuria for several hours may develop, especially in goats, the kidneys in these animals then remaining loaded with uric acid We, therefore, have to conceive of the removal of the uric acid from the organism as consisting of two separate processes, the *absorption of the uric acid from the blood and a subsequent* elimination from the kidney As shown by the clinical observations and the animal experiments together, these two processes can be injured separately

At ordinary uric acid concentrations of the blood this accumulation of uric acid in the human kidney is quite insignificant, as we had occasion to prove by several simultaneous blood and kidney tissue analyses * This evidently means that under or-

* This material was obtained at nephrectomies through the courtesy of Dr W C Quinby, of the urological service of this hospital, and it consisted

low return—three to four days for the former versus one to two days for the latter

From work in other fields we are thoroughly familiar with excretion curves of this kind Galactose, for instance, of which the greater part is utilized in the body, give rise to a sugar excretion that comes to an end in a few hours, while wholly or, at least, chiefly unusable carbohydrates Folin and Berglund[2] and Benedict and Osterberg[3] give an excretion curve that extends over several days The same inverse ratio between the degree of destruction in the body and the duration of the excretion by the urine has, in an admirable way, been demonstrated also for different amids (Fiske[4])

As to the question why the disappearance of the injected uric acid is not equally well explained as due to retention instead of destruction—to my knowledge—such an explanation for the behavior of the normal human organism has never been suggested This, of course, is no reason why it could not be so Only our experimental finding, that all the essential tissues of the body are practically impermeable for uric acid, has made the retention hypothesis lose the ground it earlier might have possessed Neither does the uric acid curve in the blood indicate retention, there is no prolonged elevation in the cases with the low elimination

We are accustomed to assume that all normal individuals react or ought to react essentially alike From the injection experiments already referred to it is clear that no strict rule of normality can be established for the handling of uric acid Some individuals have a considerably higher destructive power than others, in certain individuals there may be no destruction at all And so far as we are able to see at the present time, gout may occur just as well in one type as in another

We do not know the decomposition product or products of uric acid in the human organism This is a problem just as important as it is difficult We know, however from numerous experiments in different animals that, after uric acid injections the speed of the destruction of uric acid is roughly proportional to its concentration, the more uric acid there is present in the

of "chronic contracted kidney" or not, we have all observed that gout cases of long standing more often show a moderately damaged kidney function than they show a normal one I have, therefore, felt that any experimental contribution to this involved relationship will be received with interest, even in a purely clinical presentation

II DESTRUCTION OF URIC ACID INCREASED DESTRUCTION IN GOUT

Most investigators have observed that the daily uric acid elimination is lower in gout patients than in normal individuals This seems to be true for a sufficient number of cases to make a low endogenous uric acid output a characteristic feature of gout As to the explanation of the phenomenon, it has easily been brought into harmony with the uric acid retention concept, this latter being based upon the generally low return of uric acid in purin feeding—or injection—experiments on gout patients When we instead offer the explanation that this low endogenous uric acid in gout indicates an increased destruction of uric acid in this disease, we are well aware that we lack the support of most earlier workers in the field

We also assume a destruction of uric acid in the normal human organism, a standpoint without very much support in the modern literature But from our experiments, where we particularly avoided using as a solvent for the uric acid a substance which in itself increases the uric acid elimination, the conclusion seems a necessary one Not only did we find that young healthy individuals never excreted the full amount of uric acid that had been intravenously injected, the actual recovery varying between 30 and 90 per cent, with an average around 50 to 60 per cent, but a close analysis of the course of the elimination supports our view and helps in its further development—again in a way contrary to the accepted or expected one We have been used to speak of a "delayed" output of uric acid in gout Now it actually turns out so that the individuals who excrete the highest percentage of the uric acid injected also continue their excretion much longer than the individuals with a

ments on ducks we certainly obtained uric acid concentrations in the blood (as high as 225 mgm per 100 c c !) that theoretically are out of existence Already the uric acid concentration in the blood in uremia, though far behind the amount found in our birds, is high enough (20 to 25 mgm per 100 c c *) to conflict with the usual solubility figures The concentration in uremia is higher than any concentration ever present in gout There is, however, that great difference between these three instances that while the high concentration in ducks has been sustained only a few hours, and in uremia may last a couple of weeks, in gout it lasts for half a lifetime or more

Whatever may be the ultimate explanation, the fact remains that the gout patient with 7 mgm uric acid per 100 c c plasma shows tophi, while the normal individual with 4 to 5 5 or even 6 mgm does not

There are to be found in the human body from puberty on wide-spread abnormal deposits of other normal chemical compounds than uric acid I refer to the deposits of cholesterol esters and of lime salts in the early and advanced stages, respectively, of atherosclerosis While gout has been studied much more extensively from a chemical than from a histologic point of view, the histopathology has been almost the only line for the study of atherosclerosis, the chemical viewpoint being, in fact, of very recent date

What I want to bring out in this connection is the general nature of the interpretation of this process, as recently outlined by Aschoff,[5] in an admirable lecture, in which he goes right back to Virchow The Virchow-Aschoff theory or the "imbibition theory" requires the combination of two factors, a mechanical and a chemical one As a result of inevitable wear and tear the first manifestation of a degenerative tissue change presents itself as a loosening of the tissue elements, this being followed by an imbibition of this area with plasma At this point the chem-

* These figures indicate that there is proportionally more urea and even creatinin than there is uric acid It therefore is suggestive that we have here reached a level where there is an approximate balance between the production and destruction of uric acid in man

blood, the more rapidly is the destruction going on Applying this reasoning to our gout patients, with a constantly elevated blood uric acid, we see that, if they have any power at all to destroy uric acid, they are simply bound to destroy more uric acid than a normal person with the same intrinsic power of destruction If this factor is the only one concerned, of course, we do not know, but it offers a sufficient explanation both for the low endogenous uric acid and for the low return after uric acid injections

That these two phenomena are actually connected in this simple way is further demonstrated by a sort of reverse observation carried out on an exceptional case of gout in a young doctor of thirty This man has perfectly typical gout attacks and a constantly high uric acid level of 10 mgm in his blood, but he has no power whatsoever to destroy uric acid We first found that he had the extraordinarily high endogenous uric acid output of 1 gram a day We interpreted this as a complete absence of any destruction of uric acid and predicted a complete recovery of the uric acid we were going to inject We actually recovered 95 per cent , the best yield we have ever had

III THE URIC ACID DEPOSITS

So far there has been a positive trend in our discussion of the relationship between uric acid and gout We have built upon recognized clinical facts and upon experimental material easily accessible to control and repetition It certainly seems surprising that the first point at which we have to admit our lack of more than a hypothetic explanation is the problem of the tophi and of the uric acid deposits found on the cartilages of attacked joints

The very low solubility of the uric acid and of its sodium salts in combination with the elevation of the level of the circulating uric acid in gout seemed to offer a satisfactory explanation but there is doubt how far the test-tube experiments on the solubility of the urates are transferable to the conditions in the organism The concentration of uric acid in the urine does not harmonize with the test-tube experiments, and in our experi-

centration in the blood, coinciding with the disappearance of the symptoms, seemed to indicate a definite relationship between accumulation of uric acid and the occurrence of the attack Only, in normal individuals, after taking atophan, there was about the same extra output of uric acid as in the gout patient, the latter being the only one who was supposed to accumulate uric acid in the body, and from the work of Swift and his associates,[6] as well as of others, we know that atophan has exactly the same beneficial effect on an acutely inflamed rheumatic joint, which has nothing to do with gout or uric acid

There seems to be no doubt that, particularly during the first, more or less monarticular, period of gout acute attacks are brought about by certain dietetic excesses, but the striking thing is that it is not only purin-rich food that brings about the attacks but also a variety of other things, particularly wines and other alcoholic beverages, where we entirely fail to recognize any connection with uric acid During a later more polyarthritic stage of the disease, the acute swellings of different joints are just as clearly influenced by climatic conditions as in any chronic arthritis Thus, neither from experimental facts nor from clinical evidence is it possible to draw any positive conclusion concerning uric acid and *acute* gout

How does this influence our therapeutic procedures? The acute gout attack is, after all the symptom of gout which we are called upon to treat Our prescription of a diet low in purins is based upon sound theoretic reasoning and favorable practical experience The exclusion of a good many other things (wine, etc) from the diet is pure, but correct, empiricism

During our experiments we found that most individuals on a purin-free diet, high in protein (eggs, skimmed milk, cheese), show a lower level of circulating uric acid than on a purin-free, low protein diet (starch and cream) * The difference may

* The diet of our subjects was balanced so that it differed only in the protein content To both diets an extra amount of salt was given, originally for the sake of keeping up a fair twenty-four-hour amount of urine, even in the low protein diet (Compare Harding, V J , Allin, K D , and Van Wyck, H B , Jour Biol Chem , 1924–25, 62, 61)

ical factor comes into effect a sufficient cholesterol concentration in the plasma to produce a precipitation of the cholesterol esters in the plasma-soaked spots Aschoff virtually assumes an elevated cholesterol level of the blood during the period when these changes particularly take place

If we exchange cholesterol for uric acid and the intima of the aorta for cartilage or synovial membrane, we have a rather satisfactory hypothesis for the occurrence of uric acid deposits in gout In fact, in the so-called senile degeneration of cartilage we have the same type of an atheromatous process as just described for the aorta

Such a hypothesis is not in contradiction to the usual textbook teaching, based, I believe, on Minkowski's work, that the fully developed tissue necrosis is secondary rather than primary to the uric acid deposits Neither is it in contradiction to our experimental results, which showed that *normal* tissues in general are impermeable to uric acid But it does not explain the selective localization of the deposits to cartilage and synovial membranes

IV. THE ACUTE GOUT ATTACK. ATOPHAN THE DIETETIC TREATMENT

Of the rôle of the uric acid in the acute gout attack I can express myself very briefly owing to our rather limited knowledge on this point The acute gout attack is not accompanied by any change in the usual uric acid level in the patient's blood Another point is that intravenous injection of uric acid does not bring about any gout attack And, furthermore, when during the height of an attack uric acid was injected intravenously, causing considerable increase of the uric acid content in the joint fluid of the acutely inflamed and swollen knee, this procedure did not aggravate the symptoms, but the attack subsided during the following twenty-four hours (In fact, the patients themselves often thought that the injections had a rather good therapeutic effect) This is in contrast to the conclusions once derived from the effect of atophan in acute gout The increased uric acid elimination and the rapid drop in the uric acid con-

TABLE 1

Showing Elevated Plasma Uric Acid in All Definite Cases of Gout Notice the Last Case is the Only Woman in the Series The Diagnosis in the Last and Next to Last Cases Remains Doubtful

Case	Age	Plasma uric acid per 100 c.c	Plasma N P N per 100 c.c.	Remarks.
		Mg	Mg	
23,038, Mr G-r	70	14 7	34	
21,061, Mr K-z	38	10 7	25	
———, Dr S-n	29	9 6	24	
10,966, Mr H-n	43	9 6	46	
L I H, Mr B-e	50	9 3	49	
22,896, Mr B-th	48	9 2	34	
23,179, Mr S-ds	68	8 9	48	
23,189, Mr G-y	56	8 6	30	
———, Mr W-r	54	8 4	26	
22,874, Mr M-th	50	8 2	29	
———, Mr T-y	39	7 9	44	
———, Mr M-n	65	7 8	28	
———, Mr L-d	57	7 5	30	
21,380, Mr B-l	41	7 4	25	
———, Dr H-d	68	7 2	27	
25,021, Mr K-er	65	6 6	27	
23,231, Mr B-k	53	6 5	31	
25,114, Mr S-lon	38	5 8	35	Two cases where the diagnosis gout remains doubtful in absence of tophi
Same, a year later	39	3 5	23	
Mrs L-g		4 6	23	

figures for a number of cases of chronic arthritis of different types The number of gout cases is not great, but the table as it stands is significant enough to show that gout cases with normal blood uric acid are very scarce Since many will object to this conclusion, I feel compelled to name the symptoms which I have required for a definite diagnosis Besides a typical history, which always will remain of paramount importance, all the cases, except the 2 doubtful ones have shown either tophi or pathologically elevated plasma uric acid, or both A good many wise things have been said and written about the symptoms which constitute "a typical gout history," and in this connection I like to recall an admirable old paper by Magnus Levy,[7]

amount to as much as 2 mgm per 100 c c of plasma The high protein diet also promotes the excretion of uric acid, leaving less to be destroyed in the body Earlier we looked upon this point in quite a different way, and considered it most necessary to adhere to a low protein diet, thereby decreasing the uric acid output Whether it is the uric acid itself or its unknown decomposition products that are most harmful to the gout patient in this connection does not matter, the result of the high protein diet is equally desirable Its use is limited, however, by the often impaired condition of the kidneys in old gout cases Thus a control, in the form of non-protein nitrogen or urea determinations, against overtaxation of their functional capacity becomes necessary From the patient's personal point of view the high protein diet is more pleasant and can be made much less monotonous

V GOUT CASES WITH NORMAL BLOOD URIC ACID THE DIAGNOSIS OF GOUT THE *x*-RAY PICTURE NOT PATHOGNOMONIC

My whole presentation has been built upon the elevated level of the blood uric acid in gout Now there are clinicians in England, in Germany, and in other places who see a great many cases of gout rheumatoid arthritis, muscular rheumatism, migraine, and other headaches, and who are rather liberal with the diagnosis gout or irregular gout For many of these very experienced physicians the blood uric acid is a symptom without great significance

Furthermore, it must be freely stated that it is but recently, and practically only in this country, that the methods for the uric acid determination in blood have first become sufficiently standardized to give consistent results in the hands of clinical laboratory workers Fully consistent results will never be obtained but from plasma or serum The inevitable loss of uric acid from whole blood is too variable a factor to make whole blood determinations completely satisfactory

I insert Table 1, showing the plasma uric acid values for all the gout cases I have observed during the last three years For comparison I also show Table 2, with the corresponding

TABLE 1

Showing Elevated Plasma Uric Acid in All Definite Cases of Gout Notice the Last Case is the Only Woman in the Series The Diagnosis in the Last and Next to Last Cases Remains Doubtful

Case	Age	Plasma uric acid per 100 c.c.	Plasma N P N per 100 c.c.	Remarks.
		Mg	Mg	
23,038, Mr G-r	70	14 7	34	
21,061, Mr K-z	38	10 7	25	
———, Dr S-n	29	9 6	24	
10,966, Mr H-n	43	9 6	16	
L I H, Mr B-e	50	9 3	49	
22,896, Mr B-th	48	9 2	34	
23,179, Mr S-ds	68	8 9	48	
23,189, Mr G-y	56	8 6	30	
———, Mr W-r	54	8 4	26	
22,874, Mr M-th	50	8 2	29	
———, Mr T-y	39	7 9	44	
———, Mr M-n	65	7 8	28	
———, Mr L-d	57	7 5	30	
21,380, Mr B-l	41	7 4	25	
———, Dr H-d	68	7 2	27	
25,021, Mr K-er	65	6 6	27	
23,231, Mr B-k	53	6 5	31	
25,114, Mr S-lon	38	5 8	35	Two cases where the diagnosis gout remains doubtful in absence of tophi
Same a year later	39	3 5	23	
Mrs L-g		4 6	23	

figures for a number of cases of chronic arthritis of different types The number of gout cases is not great, but the table as it stands is significant enough to show that gout cases with normal blood uric acid are very scarce Since many will object to this conclusion, I feel compelled to name the symptoms which I have required for a definite diagnosis Besides a typical history, which always will remain of paramount importance, all the cases, except the 2 doubtful ones, have shown either tophi or pathologically elevated plasma uric acid, or both A good many wise things have been said and written about the symptoms which constitute "a typical gout history," and in this connection I like to recall an admirable old paper by Magnus Levy,[7]

TABLE 2

Showing in 19 Cases of Chronic Polyarthritis the Plasma Uric Acid Always Below Upper Normal Limit The Cases are All Typical Cases, Either Primary Chronic or Developed Out of an Acute Onset Note 11 Cases Out of 19 are Women

Case	Age	Plasma uric acid per 100 c.c.	Plasma N P N per 100 c.c.	Remarks
		Mg	Mg	
L I H, Mr D-y	55	2 2	20	
" Mrs R-n	45	2 2	21	
" Mrs Z-k	44	2 2	29	
" Mrs Rd-n	60	2 4	22	
" Mr F-n	55	2 5	27	
" Mrs D-y	50	3 3	22	
———, Mrs S-ch	40	3 6	19	
———, Mrs H-y	27	3 7	25	
———, Mrs S-ky	50	3 8	29	
———, Mrs X-y	38	3 9	19	
———, Mrs G-n	32	4 0	21	
———, Mrs H-y	45	4 0	27	
L I H, Mr B-n	37	4 1	32	
———, Mrs R-y	38	4 2	32	
———, Mr B-k	50	4 4	27	
L I H, Mr T-r	20	4 5	20	
———, Mr OB-n	45	4 8	22	
———, Mr B-e	59	5 5	29	
L I H, Mr P-s	79	5 8	39	

written some twenty-five years ago It was actually due to that paper that, in the Out-patient Department, we started to recognize as gout cases elderly men with what seemed like a polyarthritis of late onset and progressive character, who had been treated as rheumatics, for varying lengths of time

I have not mentioned the x-ray findings as one of the factors to aid in the diagnosis There is still considerable confusion concerning their differential diagnostic value in gout Were it correct—as Brugsch[8] and Munk[9] believe—that the so-called punched-out areas in the bone, in the neighborhood of the joints, always represent intraosseal tophi, we should have referred to them much earlier in this review But in spite of creditable work, by Munk, on their histologic structure, their

pathogenesis is not indisputable Their not infrequent occurrence also in cases of chronic arthritis, as demonstrated by Strangeways[10] and others,[11] as well as in cases of more obscure bone lesions, deprives these empty spaces in the film of their pathognomonic significance, and makes the interpretation, so far offered, either wrong or incomplete Unfortunately, the excellent work of Strangeways and his associates, perfectly definite in its result on this point, has remained almost unknown

Before closing allow me, if you please, a remark on a question of nomenclature We frequently meet with the expression "uric acid diathesis" From the way it is used one easily gains the impression that it is intended to signify something we do not know We are aware of no proper use of the expression other than as a synonym for gout, and as such it is better when not used

I have tried tonight to correlate experimental results with clinical facts There is for any subject always the need of a theoretic consideration Even if the theory, as usually, is incomplete, and perhaps eventually turns out to be wrong, nevertheless it might serve the useful purpose of mapping out the situation as it is today, thereby showing the points where new attacks will have to be made for the further elucidation of the problem of gout

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